Acta Poloniae Pharmaceutica – Drug Research, Vol. 75 No. 4 pp. 875–883, 2018
DOI: 10.32383/appdr/81134

ISSN 0001-6837
Polish Pharmaceutical Society

CHEMICAL TRANSFORMATIONS OF GLUCOSE IN SOLUTIONS FOR PERITONEAL DIALYSIS AFTER STERILIZATION AND DURING STORAGE

NATALIIA HUDZ[1]*, KAROLINA KORZENIOWSKA[2] and PIOTR P. WIECZOREK[2]

[1]Department of Drug Technology and Biopharmaceutics,
Danylo Halytsky Lviv National Medical University, Pekarska 69, 79010, Lviv, Ukraine
[2]Department of Analytical and Ecological Chemistry, University of Opole,
Pl. Kopernika 11, 45-040 Opole, Poland

Abstract: The objective of this work was to estimate glucose degradation products (GDPs) in solutions for peritoneal dialysis (PD) including glucose and sodium lactate based on the change of pH and absorption of ultraviolet (UV) light. Spectrophotometric and pH-metric methods were used to measure glucose degradation and transformation of GDPs in laboratory-made solutions after heat sterilization and during storage. Mechanism of transformations of GDPs in the sterilized solutions for PD during storage and spectral characteristic of 5-HMF were studied. Common features for all the batches of the tested solutions for PD after heat sterilization were a reduce in pH, increase in the absorbance in the range of 200 to 350 nm and the appearance of λ_{max} at 274-283 nm. This indicated that 3,4-dideoxyglucosone-3-ene (3,4-DGE) and 5-hydroxymethylfurfural (5-HMF) had been formed during heat sterilization. Hypsochromic shift relative to 5-HMF was explained by a spectral interference of levulinic acid having λ_{max} at 266 nm. The change of pH after sterilization depended on the initial pH (before sterilization) and glucose concentration. During storage at room temperature hypsochromic or slight batochromic shift was observed. The absorbance at 228-230 nm diminished while that at λ_{max} (270.5-280 nm) was slightly reduced or even increased depending on the composition of a solution and time of storage. It was established that 5-HMF had two absorption maxima at the wavelengths of 228-229 and 283-284 nm in the water medium and the absorbance of 5-HMF at 284 nm followed Beer's law very well in the range of concentrations of 1.97 to 9.85 mg/L.

Keywords: peritoneal dialysis, 5-hydroxymethylfurfural, 3,4-dideoxyglucosone-3-ene

Glucose is still used in the composition of solutions for peritoneal dialysis (PD), as these solutions are the first choice for the treatment of end-stage of renal failure (1). As sterility is one of the main quality indexes of solutions for PD, these solutions are undergone heat sterilization. This process gives rise to forming glucose degradation products (GDPs) including monocarbonyl and unsaturated α-dicarbonyl compounds: glucosone, 3-deoxyaldose-2-ene, 3-deoxygalactosone, 3-deoxyglucosone (3-DG), 3,4-dideoxyglucosone-3-ene (3,4-DGE), 5-hydroxymethylfurfural (5-HMF), acetaldehyde, formaldehyde, methylglyoxal, glyoxal, and low molecular acids, etc. (1-11, 13).

The level of the glucose degradation depends on its concentration, the preheating pH, and sterilization regime (heating and cooling time of an autoclave, temperature of sterilization), amount of chambers in a container, time and temperature of storage and other factors (2, 3, 5, 8-10). The process of transformation of GDPs takes place during storage as well. For example, 3,4-DGE can be formed from variety of its precursors (3-DG, enol 3-deoxyaldose-2-ene and other unidentified GDPs), especially at elevated temperatures (11), or the main part of 3,4-DGE may convert in a temperature-dependent manner to less cytotoxic compounds consisting mainly of 3-DG (reversible converting) or 5-HMF and its derivatives (irreversible converting) depending on time of storage (3, 8, 10, 11). Acidic pH and GDPs are bioincompatible with peritoneal membrane as they can induce: mesothelial cell apoptosis, a reduce of cell viability of mouse fibroblast cells L-929, NIH 3T3, human peritoneal mesothelial cells, leukocytes (2, 3, 6-8, 10, 11), impairing the enzymatic RNase A activity (7), a morphology change of mesothelial cells to a non-epitheloid phenotype, higher secretion of interleukin and vascular endothelial growth factor

* Corresponding author: e-mail: natali_gudz@ukr.net

(12), and finally cause chemical peritonitis (5). Consequently, during the pharmaceutical development of solutions for PD, it is necessary to select optimal conditions of technological process in order to reach compromise between minimization of GDPs in the solutions being developed and acceptably high pH as possible after sterilization. Spectrometric and pH-metric methods are simple, rapid and cheap to allow investigation of PD solutions at initial stages of their pharmaceutical development for the choice of sophisticated production methods such as optimizing pH of solutions, heating and cooling time of an autoclave, temperature and time of sterilization. Furthermore, these methods predict possible mechanisms of glucose degradation in a particular solution and are the basis for further studies using more sophisticated and expensive methods such as high-performance liquid chromatography.

In this work, the change of pH values and spectral characteristics of three laboratory-made batches of solutions for PD after sterilization and during storage have been investigated.

MATERIALS AND METHODS

Materials

Laboratory-made glucose solutions [sample 1 (glass containers) and sample 3 (polyvinyl chloride, PVC, containers] contained 4.25% glucose monohydrate and 40 mmol/L of lactate ions, sample 2 (glass containers) contained 2.5% glucose monohydrate and 35 mmol/L of lactate ions. Appropriate pH values were adjusted with HCl. Laboratory-made solutions were sterilized at 121°C for 15 min. Change of pH and ultraviolet (UV) absorption were used as measures of glucose degradation and transformation of GDPs. The composition of the laboratory-made PD solutions are presented in Table 1.

PVC was chosen for the study as it is the most often used for packaging of solutions for PD (2). According to literature data, glass containers are employed for the preparation of laboratory-made solutions for different studies that are explained by an easy use in laboratory conditions (10).

Chemical analysis of GDPs

5-HMF was purchased from Sigma-Aldrich (USA). It was dissolved in water before analysis (stock solution). The concentration of 5-HMF in diluted solutions was calculated upon the base of molar absorption coefficient (e) which is equal to 16.830 L • mol^{-1} • cm^{-1} at λ_{max}= 283 nm.

Methods

Spectrophotometers Photometry Hitachi U-2810 (Hitachi High-Technologies Corporation, Japan) and Optizen POP (Mecasys Co. Ltd., Korea) were used. A 1-cm quartz cell was used over the range of 200 to 350 nm.

pH values were determined by pH meters pH-410 (Aquilon, Russian Federation), pH-150 M (Gomel Plant of Measuring Instruments, Belarus) and pH/Ion meter S220 (Mettler Toledo, Switzerland) calibrated with buffers 4.01 and 6.86.

RESULTS AND DISCUSSION

After heat sterilization all the batches showed increased acidity (formation of low molecular acids during sterilization), an increase in the absorbance in the range of 200 to 350 nm (including the absorbance at 228 and 283-284 nm) and the appearance of the maximum absorption in the range of 274 to 283 nm (Table 2). This is in agreement with the data of Linden et al. (3), Erixon et al. (10, 11) and Kjellstrand et al. (8) indicating the formation of 3,4-DGE and 5-HMF from glucose during sterilization. It was found that the higher value of a pH before sterilization the bigger was the change of pH. According to the British Pharmacopeia, 5-HMF is an aldehyde that is used as an indicator for the quality of solutions for infusions and PD which contain glucose (13). The appearance of λ_{max} at 274-283 nm gave the evidence of glucose degradation, in particular, forming 5-HMF (3, 8, 9, 14). Hypsochromic shift compared to 5-HMF λ_{max} (283-284 nm) was explained by spectral interference of levulinic acid with the absorption maximum at 266 nm (14).

One of the most reactive GDPs in PD solutions is 3,4-DGE (2, 4, 6, 11). It is considered to be an

Table 1. Composition of laboratory-made solutions for PD.

No. sample	Ions concentration (mmol L^{-1})					Glucose monohydrate (g • L^{-1})	Type of containers
	Na^+	Ca^{2+}	Mg^{2+}	Cl-	Lactate		
1	132	1.25	0.25	95	40	42.5	glass
2	132	1.25	0.25	100	35	25.0	glass
3	132	1.25	0.25	95	40	42.5	PVC

Table 2. Changes in pH and spectra characteristics of the solutions for PD.

pH before sterilization	pH after sterilization	Δ pH	Absorbance of solutions			Concentration of 3,4-DGE, μmol/L	Absorbance of solutions		Concentration of 5-HMF, mg/L
			before sterilization		after sterilization				
			at λ = 228-230 nm	at λ = 273-286 nm	at λ = 228-230 nm	not standardized	at λ_{max}	at λ_{min}	≤ 9.0 mg/L (sample 2), ≤ 15.3 mg/L (sample 1 and 3)
Sample 1									
6.54	5.48	1.06	0.305 (228 nm)	0.024 (284 nm)	1.509-1.390	200	0.854 λ_{max} = 275.0	0.682 λ_{min} = 253-254	6.39
	After 44 months of storage								
	5.35	0.13	–	–	1.264-1.147	144	1.156 λ_{max} = 275.5	0.778 λ_{min} = 246.6	8.65
6.12	5.50	0.62	0.284 (228 nm)	0.014 (284 nm)	1.375-1.261	179	0.706 λ_{max} = 274.0	0.585 λ_{min} = 254	5.29
	After 44 months of storage								
	5.34	0.16	–	–	1.138-1.029	126	0.961 λ_{max} = 275.3	0.669 λ_{min} = 247.5	7.19
5.73	5.43	0.3	0.335 (228 nm)	0.034 (284 nm)	1.283-1.172	165	0.621 λ_{max} = 275.0	0.505 λ_{min} = 254-255	4.65
	After 44 months of storage								
	5.35	0.08	–	–	0.965-0.864	99	0.802 λ_{max} = 276.6	0.528 λ_{min} = 247.9	6.00
5.42	5.30	0.12	0.340 (228 nm)	0.033 (284 nm)	1.147-1.042	142	0.541 λ_{max} = 278.0	0.414 λ_{min} = 255-256	4.05
	After 44 months of storage								
	5.26	0.04	–	–	0.931-0.833	88	0.934 λ_{max} = 279.3	0.498 λ_{min} = 247.2	6.99
5.24	5.24	0	0.331 (228 nm)	0.025 (284 nm)	0.354-0.268	9	max n/d*; 0.041-0.037 at 273-286 nm	min. n/d*	0.28

Table 2. Coninued.

pH before sterilization	pH after sterilization	Δ pH	Absorbance of solutions			Concentration of 3,4-DGE, μmol/L	Absorbance of solutions		Concentration of 5-HMF, mg/L
			before sterilization		after sterilization				
			at λ = 228-230 nm	at λ = 273-286 nm	at λ = 228-230 nm	not standardized	at λ_{max}	at λ_{min}	≤ 9.0 mg/L (sample 2), ≤ 15.3 mg/L (sample 1 and 3)
			After 44 months of storage						
	5.26	0.02	–	–	0.317-0.237	2	max n/d; 0.043 at 284.4 nm	n/d	0.32
Sample 2									
6.44	5.72	0.72	0.253-0.174	0.0076-0.0082	1.428-1.324	194	0.565 λ_{max} = 278.0	0.486 λ_{min} = 258.0	4.23
	After 15 months of storage								
	5.35	0.37	–	–	0.776-0.679	74	0.482 λ_{max} = 270.5	0.386 λ_{min} = 249.5	3.61
6.05	5.65	0.40	0.259-0.179	0.0076-0.0083	1.422-1.319	194	0.527 λ_{max} = 276.0	0.459 λ_{min} = 258.0	3.95
5.72	5.57	0.15	0.258-0.178	0.0068-0.0069	1.249-1.152	166	0.385 λ_{max} = 278.0	0.335 λ_{min} = 260.0	2.88
	After 15 months of storage								
	5.26	0.31	–	–	0.624-0.542	49	0.378 λ_{max} = 275.5	0.263 λ_{min} = 250.0	2.83
5.42	5.39	0.03	0.263-0.181	0.0021-0.0029	1.190-1.095	155	0.382 λ_{max} = 281.0	0.302 λ_{min} = 260.0	2.86
	After 15 months of storage								
	5.11	0.28	-	-	0.564-0.482	39	0.340 λ_{max} = 278.0	0.211 λ_{min} = 250.5	2.55
5.21	5.21	0	0.272-0.189	0.0037-0.0046	1.139-1.045	144	0.418 λ_{max} = 283	0.288 λ_{min} = 259.0	3.13

Table 2. Coninued.

pH before sterilization	pH after sterilization	Δ pH	Absorbance of solutions			Concentration of 3,4-DGE, μmol/L	Absorbance of solutions		Concentration of 5-HMF, mg/L
			before sterilization		after sterilization				
			at λ = 228-230 nm	at λ = 273-286 nm	at λ = 228-230 nm	not standardized	at λ_{max}	at λ_{min}	≤ 9.0 mg/L (sample 2), ≤ 15.3 mg/L (sample 1 and 3)
			Sample 3						
6.47	5.63	0.84	0.290-0.203	0.017-0.0211	1.294-1.187	175	0.394 λ_{max} = 276.3	0.363 λ_{min} = 259.4	2.95
After 9 days of storage									
	–	–	–	–	1.143-1.041	147	0.379 λ_{max} =273.4	0.350 λ_{min} = 259.9	2.84
5.90	5.58	0.32	0.290-0.201	0.009-0.015	1.251-1.147	168	0.348 λ_{max} = 275.3	0.328 λ_{min} = 261.0	2.61
	After 9 days of storage								
	–	–	–	–	1.100-1.000	140	0.335 λ_{max} = 272.7	0.316 λ_{min} = 259.7	2.51
5.59	5.46	0.13	0.294-0.204	0.009-0.016	1.163-1.061	153	0.302 λ_{max} = 278.3	0.276 λ_{min} = 261.3	2.26
	After 9 days of storage								
	–	–	–	–	1.028-0.932	128	0.293 λ_{max} = 275.4	0.271 λ_{min} = 260.6	2.19
5.41	5.35	0.06	0.306-0.215	0.013-0.017	1.142-1.042	149	0.302 λ_{max} = 279.3	0.264 λ_{min} = 261.0	2.26
	After 9 days of storage								
	–	–	–	–	0.992-0.898	121	0.281 λ_{max} = 277.2	0.253 λ_{min} = 260.6	2.10
5.14	5.12	0.02	0.319-0.226	0.015-0.020	1.050-0.949	132	0.302 λ_{max} = 282.0	0.24 λ_{min} = 260.6	2.26
	After 9 days of storage								
	–	–	–	–	0.923-0.830	108	0.282 λ_{max} = 280.0	0.239 λ_{min} = 260.0	2.11

Max. or min. n/d – maximum absorption or minimum absorption were not detected

intermediate between 3-DG and 5-HMF. It was stated that it also exists in a temperature-dependent equilibrium with 3-DG, enol 3-deoxyaldose-2-ene and a variety of unidentified substances (3, 10, 11). The concentration of 3,4-DGE in conventional glucose-containing solutions for PD has been estimated to be from 9 to 125 μmol/L depending on glucose concentrations, the number of chambers in a container and storage time (3, 4, 10, 11). 3,4-DGE at these concentrations inhibits cell growth of mouse L-929 fibroblast and human peritoneal mesothelial cells, induces apoptosis of neutrophils and peripheral blood mononuclear cells that are relevant for peritoneal physiopathology and defense (2, 3, 6, 11). 3,4-DGE may react with proteins locally in the dialysate producing AGEs that are, in turn, transported into the circulation (2). The *cis*-form of 3,4-DGE has an absorption maximum at 228 nm (3, 8). 5-HMF solutions show two absorption maxima at 228-229 and 283-284 nm with A_{284} : A_{228} ratio in the range of 5.04 to 5.65 that almost conforms to the data provided by Kjellstrand et al. (8). The molar absorption coefficient of 3,4-DGE at 228 nm is 5300 L • mol^{-1} • cm^{-1}, 5-HMF at 228 nm is 3000 L • mol^{-1} • cm^{-1}, at 284 nm is 17000 L • mol^{-1} • cm^{-1} (8). Literature data on the molar absorption coefficient of 5-HMF differ. Zhang et al. (14) provide it as 22700 L • mol^{-1} • cm^{-1} at 284 nm and USP gives 16830 L • mol^{-1} • cm^{-1} at 283 nm (14, 16). For calculation of 5-HMF concentration ($X_{5\text{-HMF}}$), in mg/L, in the solutions of 5-HMF and the tested solutions for PD, we employed the following formula:

$$X_{5\text{-HMF}} = A : 16830 \cdot 126 \cdot 1000,$$

where A – absorbance of a solution at λ_{max}, 16830 – molar absorption coefficient in L • mol^{-1} • cm^{-1} at 283 nm, 126 – molar weight of 5-HMF, 1000 – recalculation on mg.

The extent of finding 5-HMF in its solutions was in the range of 94.19 to 98.95%. It was found that the absorbance of 5-HMF at 283-284 nm follows Beer's law in the concentration range of 1.97 to 9.85 mg/L ($y = 0.124 \cdot x + 0.0158$, $R^2 = 0.999$). The accepted maximum concentrations of 5-HMF in the solutions for PD were calculated on the base of the requirements of the British Pharmacopeia: not more 10 μg of 5-HMF for 25 mg glucose.

The absence of the absorption maximum at 228-230 nm in the solutions for PD after sterilization is explained with spectral interferences of lactate ions and levulinic acid. Glucose does not give spectral interferences (Fig. 1). The spectra of levulinic acid provided in Zhang et al. (14) paper confirm this assumption. UV absorption of lactate overlays the absorption band of 5-HMF and 3,4-DGE up to 230 nm. For calculation of 3,4-DGE concentration ($X_{3,4\text{-DGE}}$) in the tested PD solutions, we used the principle applied by Kjellstrand et al. (8). Assuming that all the absorbance at the maximum is due to 5-HMF, 1/5.7th of the absorbance at the absorption maximum and the absorbance caused by lactate (approximately 0.3) may be subtracted from the total absorbance at 228 nm. Our studies confirm the value of 0.3 as the absorbance of the solutions before sterilization at 228 nm which was in the

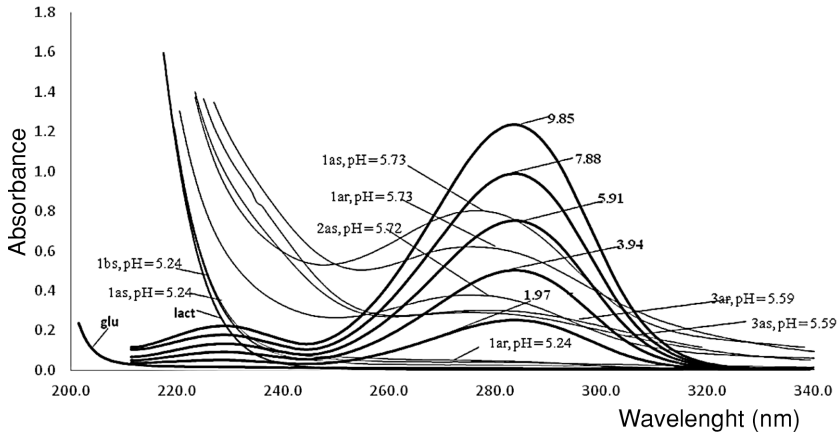

Figure 1. Spectra of the tested samples and solutions of 5-HMF, 1bs, 5.24 – sample 1 with pH = 5.24 before steam sterilization, 1ar, 5.24 – sample 1 with pH = 5.24 after steam sterilization, 1as, 5.24 – sample 1 with pH = 5.24 after storage of 44 months, 1ar, 5.73 – sample 1 with pH = 5.73 after steam sterilization, 1as, 5.73 – sample 1 with pH = 5.73 after storage of 44 months,as, 5.72 – sample 2 with pH = 5.72 after storage of 15 months, 3ar, 5.59 – sample 3 with pH = 5.59 after steam sterilization, 3as, 5.59 – sample 3 with pH = 5.59 after storage of 9 days,1.97, 3.94, 5.91, 7.88, and 9.85 – solutions of 5-HMF in concentrations of 1.97, 3.94, 5.91, 7.88 and 9.85 mg/mL, gluc – 4.25 % solution of glucose monohydrate,lact – solution of sodium lactate (40 mmol/L)

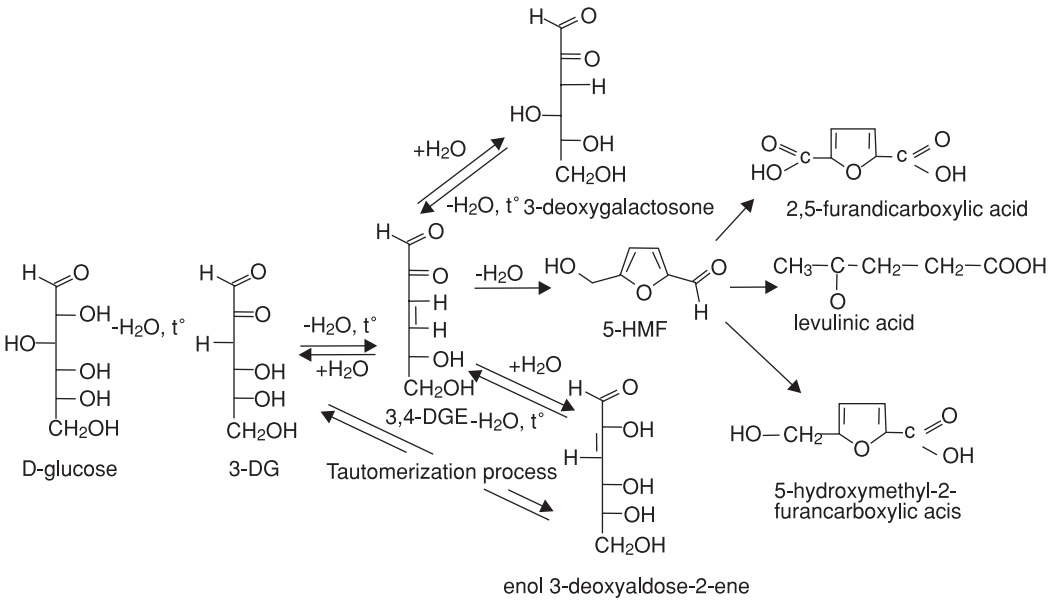

Figure 2. Scheme of converting glucose and the main GDPs

range of 0.253 to 0.340. Therefore, the remaining part of the absorbance at 228 nm will then be due mainly to 3,4-DGE, and will be denoted as $A_{228corr}$ = $[A_{228} - (A_{\lambda max} : 5.7) - 0.3]$. Concentration of 3,4-DGE, in µmol/L, was calculated according to the following formula:

$$X_{3,4\text{-DGE}} = A_{228corr} : \varepsilon \bullet 1000\,000 =$$
$$A_{228corr} : 5300 \bullet 1000\,000 = A_{228corr} \bullet 188.68.$$

Kjellstrand et al. (8) stated that $A_{228corr}$ was considered to be predictors of potential adverse clinical reactions as it was more suitable and easily handled compared with a determination of inhibition of cell growth. Table 2 demonstrates that the content of 3,4-DGE immediately after sterilization and during storage was in the range of 9 to 200 µmol/L and 2-147 µmol/L, respectively. This is almost in line with works of Erixon et al. (2004, 2009), Santamaria et al. (2008) and Ortiz et al. (2011) (2, 4, 6, 10). Erixon et al. (2004) determined content of this substance as 125 and 25 µmol/L in the laboratory-made solution with glucose and lactate concentrations of 1.5% and 35 mmol/L, and pH 5.5 before sterilization immediately after sterilization and 30 days of the following storage, respectively (10). It should be noted that up to now there is no regulation for the content of 3,4-DGE in solutions for PD.

After 44 months of storage of the solutions of sample 1 at room temperature the values of pH reduced (0.13-0.04). After storage during 44 months of the solutions of sample 1 with exception of the solution with pH 5.24 before sterilization, a slight bathochromic shift of the wavelength of the maximum absorption took place. The absorbance at 228-230 nm diminished while at the maximum 275.3-279.3 nm increased and, respectively, the concentration of 3,4-DGE decreased and 5-HMF increased (Table 2). This is all in agreement with Kjellstrand et al. (8) who reported that levels of GDPs absorbing at 228 nm (including 3,4-DGE) decreased, but, in contrast, the absorbance at 284 nm (caused mainly by 5-HMF) increased during the storage.

After 15 months of storage at room temperature, the values of pH of the solutions of sample 2 were reduced. The pH change was in the range of 0.37 to 0.28. A hypsochromic shift was characteristic for the wavelength of maximum absorption. The absorbance at 228-230 nm diminished while that at the absorption maximum was lowered (Table II). This also indicated that a transformation of GDPs had taken place in the process of storage of the solutions for PD but a mechanism of the transformation seemed to differ from the solutions of sample 1. A reduction of the absorbance at 228 nm without a notable increase concentration of 5-HMF is agreed with hypotheses of Erixon et al. about not necessary an increase of 5-HMF concentration at a decrease of 3,4-DGE concentration as 5-HMF may have further been degraded (10).

After 9 days of storage at room temperature, the maximum absorption shifted hypsochromically.

The absorbance at 228-230 nm diminished while that at the maximum at 272.7-282.0 nm was slightly reduced (Table 2). This indicated that during the first week concentration of 3,4-DGE decreased. This fact harmonizes with the data of Erixon et al., who even recommended not to use solutions for PD soon after sterilization with the purpose of avoiding exposure of patients to higher levels of 3,4-DGE immediately after sterilization (10).

Table 2 also demonstrates one more regularity: the higher was pH after sterilization the higher was content of 3,4-DGE. All the solutions after sterilization met the requirements of British Pharmacopeia for pH and content of 5-HMF. To our mind, it is necessary to carry out cytotoxicity studies in order to establish a compromise between maximally accepted pH and lower content of 3,4-DGE after sterilization.

Figure 1 demonstrates that the spectra of all the solutions with exception of sample 1 with pH 5.24 are similar and do not depend on glucose and sodium lactate concentration and type of packaging. The following one more regularity was established: the higher pH before sterilization the longer hypsochromic shift was observed at the absorption maximum. The spectra of the solution of sample 1 with pH = 5.24 before thermal sterilization, after sterilization and storage of 44 months put each other because there is no glucose degradation. The absence of degradation in some solutions which are concomitantly sterilized could be explained by gentle conditions of the sterilization, namely, by a brief time of heating to temperature sterilization (121^{o}C) and cooling autoclave after sterilization. In this case, there is not enough energy for a converting of glucose into 3-DG and latter into 3,4-DGE in all the containers (10).

Finally, on the base of own studies and literature data we presented the scheme of converting glucose and the main GDPs. This scheme shows that glucose degradation processes occur during heat sterilization of the tested solutions for PD. However, these processes do not stop after sterilization. GDPs transformation processes take place during storage at room temperature. These processes should be taken into consideration at characterizing quality of solutions for PD after sterilization and during storage.

CONCLUSIONS

Processes of glucose degradation and converting GDPs in solutions for PD occur during sterilization and storage. Direct UV spectrometric and potentiometric methods are simple, cheap and rapid and have potential to estimate converting processes in solutions for PD during their pharmaceutical development and routine manufacture. We have confirmed that immediately after sterilization levels of 3,4-DGE in solutions for PD are high. During storage levels of 3,4-DGE gradually diminish while pH of solutions reduces and concentrations of 5-HMF reduce or increase depending on time of storage and composition of solutions. As it is not fully understandable which GDPs and acidic values of pH are related with cytotoxicity, it is advisable to conduct studies for determination of cytotoxicyty of PD solutions depending on pH before sterilization.

Finally, there is a large variation of concentrations of 3,4-DGE depending on pH before sterilization and time of storage (2-200 μmol/L). pH before sterilization is the main factor influencing the content of GDPs. The content of 3,4-DGE and 5-HMF (using molar absorption coefficients 5300 at 228 nm and 16830 L • mol^{-1} • cm^{-1} at $\lambda_{max,}$ respectively) in solutions for PD may be estimated by quick measurement of pH, the absorbance at 228 nm, corrected for the presence of lactate and 5-HMF, and at λ_{max}, respectively.

In conclusion, the scheme of converting glucose and the main GDPs is presented on the base of own studies and literature data.

Acknowledgements

Coauthor N. Hudz is grateful to the International Visegrad Fund for providing a scholarship for the research as this paper was created during the contracted research project 51700107.

REFERENCES

1. Diaz-Buxo J.A., Sawin D.-A., Himmele R.: Dialysis Transplant. 40, 356 (2011).
2. Ortiz A., Santamaria B., Montenegro J.: Biocompatible Solutions for Peritoneal Dialysis, Progress in Peritoneal Dialysis, Dr. Ray Krediet (Ed.), 2011, ISBN: 978-953-307-390-3, InTech.
3. Linden T., Cohen A., Deppisch R., Kjellstrand P., Wieslander A.: Kidney Int. 62, 697 (2002).
4. Tomo T., Okabe E., Yamamoto T., Namoto S., Iwashita T. et al.: J. Artif. Organs 10, 47 (2007).
5. Adib N., Shekarchi M., Hajimehdipoor H., Shalviri G., Shekarchi M., Imaninejad M.: Iran. J. Pharm. Res. 10, 113 (2011).
6. Santamarıa B., Ucero A.C., Reyero A., Selgas R., Ruiz-Ortega M. et al.: Nephrol. Dial. Transplant. 23, 3307 (2008).

7. Distler L., Georgieva A., Kenkel I., Huppert J., Pischetsrieder M.: Chem. Res. Toxicol. 27, 1421 (2014).
8. Kjellstrand P., Erixon M., Wieslander A., Lindén T., Martinson E.: Perit. Dial. Int. 4, 385 (2004).
9. Gudz' N.: Vest. Farm. 68, 33 (2015).
10. Erixon M., Linden T., Kjellstrand P., Carlsson O., Ernebrant M. et al.: Perit. Dial. Int. 4, 392 (2004).
11. Erixon M., Wieslander A., Linden T., Carlsson O., Forsbäck G. et al.: Perit. Dial. Int. 6, 583 (2005).
12. Fernández–Perpén A., Pérez–Lozano M.L., Bajo M.–A., Albar–Vizcaino P., Correa P.S. et al.: Perit. Dial. Int. 3, 292 (2012).
13. British Pharmacopoeia. Edition 2009, p. 10952, The Stationery Office, London 2009.
14. Zhang J., Li J., Tang Y., Xue G.: Sci. World J. article ID 506329 (2013); https:// doi.org/ 10.1155/2013/506329.
15. Erixon M., Wieslander A., Lindén T., Carlsson O., Jönsson J.A. et al.: Perit. Dial. Int. 29, 28 (2009).
16. Polydextrose: http://www.drugfuture. com/ Pharmacopoeia/usp35/PDF/1896-1898%20 Polydextrose.pdf (accessed on 15.10.2017).

Received: 15. 10. 2017