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Size exclusion chromatography with evaporative light scattering detection as a method for speciation analysis of polydimethylsiloxanes. II. Validation of the method for analysis of pharmaceutical formulations

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ABSTRACT

The aim of this study was to demonstrate the usefulness of the size exclusion chromatography with evaporative light scattering detection (SEC-ELSD) method in the identification and quantitative analysis of polydimethylsiloxanes (PDMS). The process of validation for the method was conducted, and the values obtained were compared with the acceptance criteria. Particularly important was the conclusion that SEC-ELSD method showed a high specificity for PDMS. PDMS is an organosilicon polymer and for this reason, it does not exist as a concrete chemical species. Depending on the length of the chain, PDMS can be toxic for organism. So far, the SEC-ELSD method has not been applied for the control of pharmaceutical products containing such PDMS as dimeticone or simeticone. The safety of use and effectiveness of such pharmaceutical products relies on the control of their quality. Therefore, the analytical methods and procedures that meet acceptance criteria for qualitative and quantitative analysis of the PDMS should be used. In the case of the analysis of pharmaceutical products, the acceptance criteria are established and recommended by, for example, the Pharmacopoeias, the U.S. Food and Drug Administration (FDA), the International Conference on Harmonisation (ICH) and the World Health Organization (WHO). The progress of knowledge, however, requires the development of new analytical tools which are able to solve incoming problems. In the case of pharmaceutical formulations containing PDMS, which are used not only by adults but also by children, it is necessary to use analytical methods which are characterized by a high specificity.

1. Introduction

The validation process is one of the most important stages of the development of new analytical methods or procedures. The usefulness of an analytical method or procedure is based on the values of validation parameters [1–6]. The aims of the validation are many aspects which depend on the individual analytical strategy and the specific purpose of an investigation (Fig. 1).

The validation process and acceptance criteria should be clearly defined for an analytical method which is used for the control of any pharmaceutical products. Both the method and the analytical procedure must ensure the effectiveness of pharmaceutical product, expressed as a suitable content of the active pharmaceutical ingredients (API) measured by means of quantitative analysis, as well as the safety of drug (qualitative analysis of API) and also the adequate drug quality (the content of impurities in the final product below the level allowed – qualitative and quantitative analysis). Guidelines for the evaluation of safety, effectiveness and quality of pharmaceutical products were developed at the International Conference on Harmonization (ICH) (Requirements for Medicinal Products) [7]. The document regarding the validation process for method and analytical procedure was published as the guideline ICH Q2 R1 [7]. Information regarding the validation procedures has also been mentioned in the report of the World Health Organization (WHO) [8], in e.g. the European (EP) [9] and U.S. (USP) [10] Pharmacopoeias, as well as by the U.S. Food and Drug Administration (FDA) [11]. There is a great number of recommended validation parameters which concern both identification and quantification of analytes (Table 1). As it is shown in Table 1, the strategy of validation which was adopted by the different organizations is very similar, though there are a few minor discrepancies.

The aim of this study was to validate the size exclusion chromatography with evaporative light scattering detection (SEC-ELSD) method [12,13] and to evaluate the usefulness of this method for

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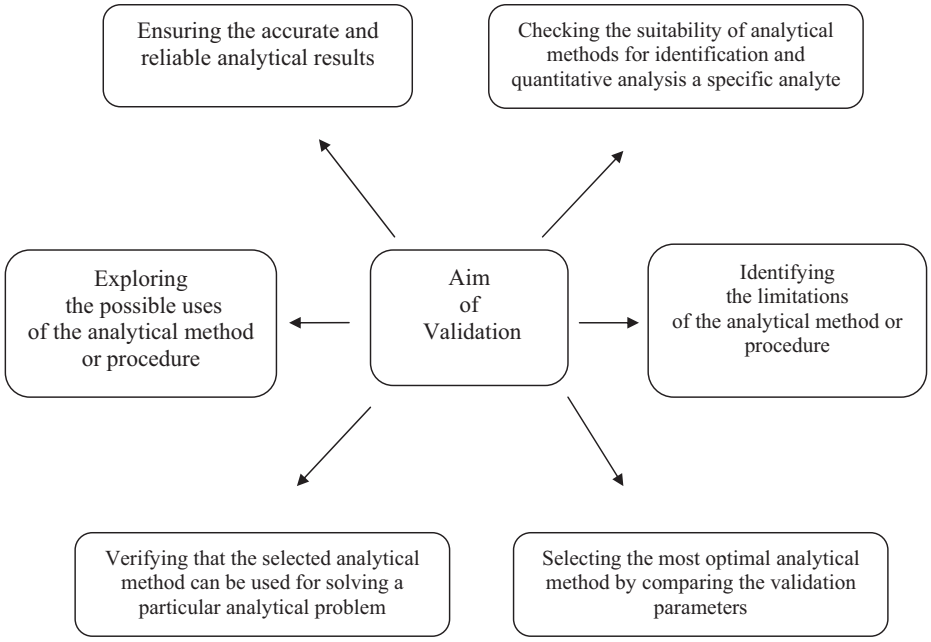

Fig. 1. The aim of validation.

polydimethylsiloxanes (PDMS) analysis. So far, this method has not been used for identification and quantification of PDMS in pharmaceutical products. PDMS is used as an active pharmaceutical ingredient which is called dimeticone or simeticone (if contains SiO_2).

The infrared spectroscopy (FTIR and IR), recommended by the European and American Pharmacopoeia [14,15], is not sufficiently specific for PDMS and it is therefore reasonable to search for other analytical techniques. The specificity of a method is a very important validation parameter, because it guarantees that the method examined is suitable for identification of the defined analyte. Some authors claimed that the polymerization degree (which determines the viscosity and molecular weight) or the chemical structure (linear or cyclic) of PDMS can affect their migration and absorption in the organism, as well as their toxicity. For this reason the high specificity of the analytical method is crucial [16–20].

The quality control of pharmaceutical products requires confirmation of both the identity and the quantity of the active substance in the dosage form. The validation of the analytical procedure provides the selection of the most optimal method for a high quality control of a product. Therefore that the SEC-ELSD method has not been used for control of pharmaceutical formulations containing PDMS so far, the validation process did not rely only on the guidance given in pharmacopoeias [9,10], but also on other strategies for validation [7,8,11].

2. Experimental

2.1. Instrumentation and chromatographic conditions

An ELSD detector (BBT Automatyka, Gdansk, Poland), an isocratic pump (mini Star K 500, Knauer, Germany), a manual

Table 1
Validation parameters recommended by ICH, WHO, EP, USP and FDA.

Validation parameter		ICH	WHO	EP	USP	FDA	
Qualitative analysis (identification)	Selectivity	–	–	The methods present in monographs and general chapter were validated in accordance with accepted scientific practice and actual recommendations for the validation of analytical methods. If it is not tick otherwise in the monographs or general chapter the validation of methods is not required.	–	–	
	Specificity	+	+		+	+	
	Accuracy	–	–		–	–	
	Trueness	–	–		–	–	
	Precision	–	–		–	–	
	Repeatability	–	–		–	–	
Quantitative analysis	Range	+	+		+	+	
	Linearity	+	+		+	+	
	Precision						
	Repeatability	+	+			+	+
	Intermediate precision	+	+			+	+
	Reproducibility	+[a]	–			–	+[a]
	Accuracy	+	+		+	+	
	Trueness	–	–		–	–	
	Limit of detection	–	+		+	–	
	Limit of quantification	–	+		+	–	
	Robustness	–	+		+	+	
	Ruggedness	–	–		+	–	

ICH, International Conference on Harmonisation; WHO, World Health Organization; EP, European Pharmacopoeia; USP, United States Pharmacopoeia; FDA, Food and Drug Administration.

[a] Do not need to set the intermediate precision, if reproducibility was determined.

injector with 20 μl loop (Knauer, Germany) and a TSK–GEL $H_{HR}GMH_{HR}$–M column with polystyrene-divinylobenzen packing (5 μm, 300 mm × 7.8 mm) from the Tosoh Biosep company (Poznan, Poland) were used for the method development. Data acquisition, analysis, and reporting were performed using the Eurochrom 2000 (Knauer, Germany) software. The following conditions were used [12]: mobile phase – chloroform; flow rate of the mobile phase – 1 ml/min; carrier gas pressure (CO_2) – 140 kPa; temperature of the drift tube – +50 °C.

2.2. Materials and chemicals

Polydimethylsiloxanes (PDMS) with a viscosity of 10, 350 and 60,000 cSt were purchased from Sigma–Aldrich (Poznan, Poland) and used in this study. To assess the accuracy of molecular weight determinations, a standard PDMS (93,700 Da) from Aldrich Chemical Company (Poznan, Poland) was used.

For calibration of the column, three mixtures of polystyrene standards (Sigma–Aldrich, Poznan, Poland) were used, with each vial containing four certified polymers standard with molecular weight ranging from 376 to 2,570,000 Da. The chloroform was HPLC grade and also purchased from Sigma–Aldrich (Poznan, Poland). Disposable syringe filters (Chromafil PET-45/25 Macherey-Nagel, Germany) were used for samples preparation.

2.3. Formulation

The pharmaceutical product used in this study was Manti Gastop (US Pharmacia Wroclaw, Poland) – chewable tablets, containing 125 mg simethicone per tablet.

Table 2
Parameters used for validation of the analytical methodology.

Qualitative analysis (identification)	Quantitative analysis
	-Range
	-Linearity
-Specificity	-Sensitivity
-Accuracy/trueness	-Precision/repeatability/intermediate precision
-Precision/repeatability	-Accuracy/trueness
	-Limit of detection
	-Limit of quantification

2.4. Preparation of samples

A PDMS standard was prepared as a 5% chloroform solution. Next, the polystyrene standards were prepared by adding to each vial 0.375 ml chloroform to obtain final concentrations of 0.134 and 0.268%. Following the manufacturer's instructions, the mixture was kept for 2 h in room temperature to allow the mixture of polystyrenes to dissolve entirely.

Samples of Manti Gastop tablets were prepared in accordance with the US and European Pharmacopoeias [14,15,21]. Two tablets were placed in a conical flask with 25 ml of dilute (2:5) HCl and 25 ml chloroform and extracted for 10 min. Samples were taken with a syringe from both the lower (containing simeticone in chloroform) and the upper layer to control of 'matrix'. The both layers were filtered through a 0.45 μm syringe filter. The recovery tests for PDMS from matrix of tablets Manti Gastop were prepared in a similar way.

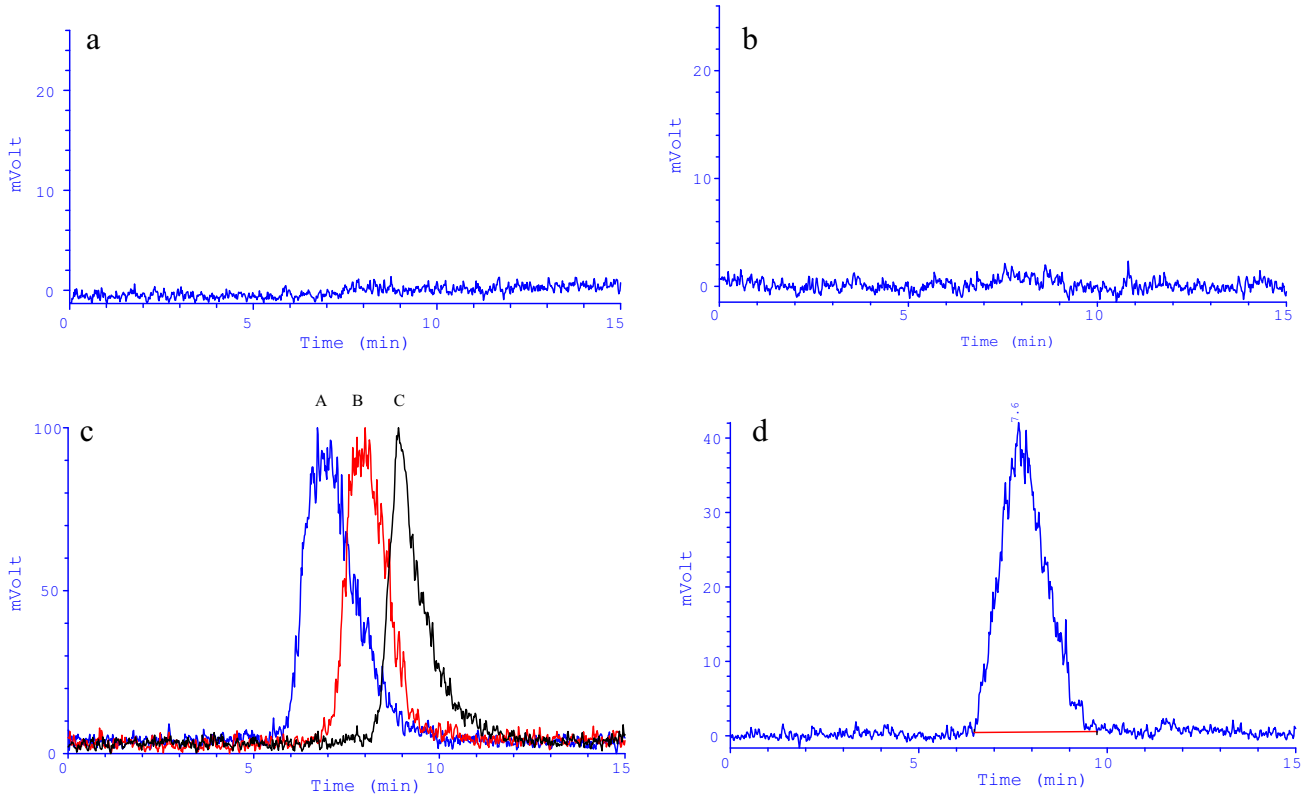

Fig. 2. (a) Chromatogram of blank. (b) Chromatogram for a chloroform extract of the matrix of Manti Gastop tablets. (c) Superimposed chromatograms for chloroform solutions of polydimethylsiloxanes with viscosities of 10 cSt (C), 350 cSt (B) and 60,000 cSt (A). (d) Chromatogram for a chloroform extract of Manti Gastop tablets.

Table 3
Mean retention times and molecular weights for PDMS with a viscosity of 10, 350 and 60,000 cSt, and for a chloroform extract of Manti Gastop tablets.

Sample	Retention time average value $n = 5$ [min]	Molecular weight [Da]
PDMS – 10 cSt	9.12	1263
PDMS – 350 cSt	7.75	17,523
PDMS – 60,000 cSt	6.95	81,373
Manti Gastop – chewable tablets	7.81	15,617

Table 4
Evaluation of the precision of the SEC-ELSD method used to qualitative analysis of PDMS, on the basis measurements PDMS standard 93,700 Da.

Parameter	Retention time [min] average value $n = 10$ confidence interval $\alpha = 0.05$	Molecular weight [Da] average value $n = 10$ confidence interval $\alpha = 0.05$
Precision RSD [%]	6.89 ± 0.040 0.53	$91{,}519 \pm 6968$ 3.04

3. Results and discussion

3.1. Stages of SEC-ELSD validation process

The validation process, of the presented method, consisted of three stages:

- the formulation of the issue which allowed to determine the expectations and demands for the SEC-ELSD method, in accordance with acceptance criteria;
- the choice and determination of the parameters of validation (Table 2);
- the evaluation of usefulness of the SEC-ELSD method for qualitative (identification) and quantitative analysis of polydimethylsiloxanes which are present in various pharmaceutical formulations.

The assessment of the suitability of SEC-ELSD method for polydimethylsiloxanes analysis was based on acceptance criteria adopted from guidance [3,4,7,23–26].

3.2. Parameters of validation for the qualitative analysis

3.2.1. Evaluation of specificity of the method

The specificity of a method indicates the possibility of the application of an analytical method or procedure for to identification of concrete component (analyte). The specificity guarantees that the signal of the analyte can be distinguished from the signal obtained from a matrix. The validation of this parameter can be carried out by analysis of a placebo sample, i.e. the pure matrix, followed by a comparison of the results obtained with those from a sample containing the analyte. The blank sample should not produce a signal which is characteristic for the analyte. In the case of chromatographic techniques, the specificity of the method can be determined on the basis of the retention time and control the matrix. Fig. 2a presents the chromatogram obtained for a blank sample which was prepared by shaking 25 ml of chloroform with 25 ml of distilled water and diluted hydrochloric acid (2:5), where in Fig. 2b the chromatogram obtained for a chloroform extract of the matrix in Manti Gastop tablets is given. Fig. 2c presents chromatograms obtained for PDMS with viscosities 10, 350, 60,000 cSt, which were dissolved in chloroform, and in Fig. 2d the chromatogram obtained for an extract of a pharmaceutical formulation (Manti Gastop) is showed.

While comparing the different chromatograms obtained, it can be concluded that the peaks in Fig. 2c and d originated from the polydimethylsiloxanes with different molecular weight (and thus viscosity). The specificity of the analytical procedure was verified by analyzing both a blank sample and the matrix of the Manti Gastop (Fig. 2a and b), and no peaks occurred at retention times corresponding to the designated PDMS (Fig. 2c).

In the case of the SEC-ELSD method the specificity is in accordance with not only a retention time but above all with a molecular weight of the compounds analysed. The determination of a molecular weight was necessary for a calibration of chromatographic column. In this study, the chromatographic column was calibrated with the use of 12 certified polystyrene standards with a molecular weight range from 376 to 2,570,000 Da. The relationship determined between logarithm of the mass peak M_p and the retention time t_r was: $\log \mathrm{Mp} = -0.8336\, t_r + 10.704$, with a coefficient of determination $R^2 = 0.9938$. This equation was used to assess the mean molecular weight for each specific PDMS (Table 3).

3.2.2. Evaluation of precision, repeatability, accuracy and trueness of the qualitative analysis

For the credibility of the method it is important to evaluate the precision, accuracy and trueness of the molecular weight determination. This evaluation was carried out using a PDMS standard with a molecular weight of 93,700 Da as specified by the manufacturer (Tables 4 and 5). This value was considered as the actual value, and the calculated relative error was used for measurement of accuracy and trueness (Table 5). The precision of the method was expressed as a relative standard deviation (RSD) for both retention time and molecular weight (Table 4). The confidence intervals for different retention times and estimated values of molecular weight were calculated (the level of significance: $\alpha = 0.05$, the number of degrees of freedom: $r = n - 1$, where $n = 10$; Table 4).

Based on the results for the PDMS standard with the molecular weight 93,700 Da it was concluded that even unknown molecular weight for different PDMS can be determined using a calibration

Table 5
Evaluation of the accuracy and trueness of the SEC-ELSD method used to qualitative analysis of PDMS, on the basis measurements PDMS standard 93,700 Da.

Parameter	Retention time [min]	Molecular weight [Da]	Relative error [%]
Accuracy single measurement $n = 1$	6.90	89,569	−4.41
Trueness average value $n = 10$	6.89	91,519	−2.33

Table 6
Evaluation of the precision and repeatability of the SEC-ELSD method used to qualitative analysis of PDMS, on the basis measurements PDMS standard 350 cSt.

Parameter	Concentration PDMS [%]	Retention time [min] average value $n = 7$ confidence interval $\alpha = 0.05$	RSD [%]
Precision	0.3	7.79 ± 0.08	0.40
	0.5	7.77 ± 0.19	0.98
	0.8	7.78 ± 0.16	0.86
Repeatability			0.75

Table 7
Results integrated peak areas and relative standard deviation for different concentrations of PDMS determined by SEC-ELSD.

Concentration PDMS 350 cSt [%]	Integrated peak area [mV min]							Integrated peak area average value [mV min]	RSD [%]
	Number of measurement								
	1	2	3	4	5	6	7		
0.1	6.65	6.27	6.59	6.54	6.53	6.22	6.41	6.46	2.56
0.2	14.18	13.61	13.52	13.48	13.67	13.22	14.15	13.69	2.59
0.3	22.61	22.17	21.53	22.91	22.49	22.64	21.99	22.33	2.11
0.4	28.93	29.84	29.13	30.68	30.07	30.60	30.74	29.99	2.47
0.5	36.17	36.71	36.86	36.61	36.97	36.97	35.80	36.58	1.21
0.6	42.92	42.31	43.21	43.19	43.44	42.69	42.72	42.92	0.89
0.7	49.10	48.52	50.09	47.94	4.90	49.67	47.62	48.83	1.82
0.8	54.27	54.65	54.41	53.98	5.94	54.14	55.43	54.54	0.93
0.9	62.0	61.34	62.38	60.02	61.11	61.96	59.16	61.23	2.08
1.0	66.7	66.41	67.91	65.77	65.15	67.67	68.13	66.78	1.71

Table 8
Evaluation of the precision and repeatability of the SEC-ELSD method used to quantitative analysis of PDMS, on the basis measurements PDMS standard 350 cSt.

Parameter	Concentration PDMS [%]	Integrated peak area average value $n = 7$ [mV min]	RSD [%]
Precision	0.3	22.33	2.11
	0.5	36.58	1.21
	0.8	54.54	0.93
Repeatability			1.42

curve prepared for polystyrene standards. The value of molecular weight resulting from this methodology will have only a slight error. The accuracy of the method was −4.41%, while the trueness was −2.33%. The method of qualitative investigation (identification) also presented a high precision, which was expressed as the repeatability of the results. The relative standard deviation (RSD) for the retention time and the calculated molecular weight was 0.53% and 3.04%, respectively.

Furthermore, the repeatability of the method was measured. Those experiments were carried out using 3 different concentrations of PDMS standard with viscosity of 350 cSt: 0.3, 0.6 and 0.9% (Table 6). For each concentration seven consecutive, independent measurements were performed. Retention times obtained were highly reproducible with a RSD of less than 1%.

3.3. Parameter of validation for the quantitative analysis

3.3.1. Evaluation of range and linearity of the method

The linearity of the method was determined using a PDMS standard with a viscosity of 350 cSt. In the previous studies [22] it was demonstrated that the signal intensity is independent from the molecular weight of PDMS, and therefore a standard curve can be prepared with a PDMS of any viscosity. Ten standard solutions were prepared with the following concentrations: 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9 and 1.0%. Each solution was analysed sevenfold, using the integrated peak area for the standard curve calculation (Table 7; Fig. 3).

There was a linear relationship between the peak area and the concentration analysed, expressed as a linear regression with a very high regression coefficient, $R^2 = 0.9958$. This proves the high linearity of the detector in the range of 0.1–1% PDMS.

3.3.2. Evaluation of precision, repeatability, and intermediate precision of the quantitative analysis

Determination of precision, repeatability and intermediate precision of the method in quantitative analysis was carried out for three following concentrations: 0.3, 0.5 and 0.8%, of a standard PDMS solution with a viscosity of 350 cSt. For each concentration, 7 independent measurements were performed. The results showed that the method is characterized by a high precision (Table 8). For the concentrations 0.5 and 0.8% the precision was similar (about 1%), whereas for the lowest concentration it was over 2%. The repeatability of the method for the quantitative analysis was 1.42%.

To determine the intermediate precision, standard solutions with PDMS concentrations of 0.3, 0.5 and 0.8% were analysed at weekly intervals during one month, with three independent measurements each time. The results obtained each week and the mean value of the relative standard deviation (RSD) are summarized in Table 9. The intermediate precision was 4.26%. While comparing the RSD values (Table 8) one can notice that the variation increased

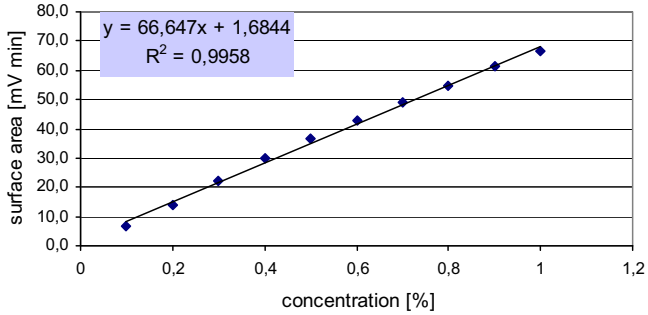

Fig. 3. Dependence of the integrated peak area on the PDMS concentration (calibration curve).

Table 9
Evaluation of the intermediate precision and repeatability of the SEC-ELSD method used to quantitative analysis of PDMS, on the basis measurements PDMS standard 350 cSt.

Concentration PDMS [%]	Integrated peak area [mV min]			Integrated peak area average value [mV min]	Repeatability RSD [%]
	Week 1	Week 2	Week 3 Week 4		
0.3	24.20	22.57	21.99	23.57	5.00
	23.00	23.11	25.50		
	25.22	23.56	23.84		
	24.75	23.27	21.87		
0.5	36.97	35.89	35.00	36.87	4.66
	40.07	39.59	37.67		
	38.24	35.57	36.60		
	36.36	34.84	35.58		
0.8	54.94	54.14	55.43	55.90	3.13
	59.28	57.25	58.40		
	55.81	55.94	56.07		
	54.24	53.25	56.09		
Intermediate precision RSD [%]					4.26

Table 10
Evaluation of accuracy and trueness of the SEC-ELSD method used to quantitative analysis of PDMS.

No.	PDMS added [mg]	Integrated peak area average value [mV min]	RSD [%]	PDMS recovery [mg]	PDMS Recovery average value [mg] Recovery [%]
1.	200.0	38.45	1.44	205.16	206.17
2.		38.70		206.52	
3.		38.75		206.84	103.09
4.	200.0	37.55		200.12	200.75
5.		37.97		202.46	
6.		37.47		199.66	100.37
7.	200.0	38.81		207.18	207.01
8.		38.88		207.58	
9.		38.65		206.28	103.51
% Recovery average value					102.32
Trueness $n = 9$ relative error [%]					+2.32

about threefold over time. Therefore, it can be concluded that the analyses should be performed within a short time period. Intermediate precision expresses the highest variability.

3.3.3. Evaluation of accuracy and trueness of the quantitative analysis

The accuracy is the degree of conformity between the result obtained from a single measurement and the expected (actual)

Table 11
Evaluation of the detection and quantification limits and sensitivity of the SEC-ELSD method used to analysis of PDMS.

Parameter	Concentration [%]
Limit of detection	0.03
Limit of quantification	0.08
Sensitivity	0.02

Table 12
Parameters of validation and criteria acceptance for the qualitative analysis polydimethylsiloxane by SEC-ELSD.

Parameter of validation	Value/commentary	Criteria acceptance
Specificity	-No interference with matrix -No peak from the matrix -The different retention times for PDMS with varying degrees of polymerization, of which can calculate the molecular weight according to the formula: $M_p = -0.8336\ t_r + 10.704$ $r^2 = 0.9938$	-Effect of interfering substances of matrix $\leq$1% -The different retention times for PDMS with varying degrees of polymerization, of which can calculate the molecular weight
Precision % (retention time)	0.53	-Lack of guidelines -Adopted $\leq$2
Precision % (molecular weight)	3.04	- lack of guidelines -Adopted $\leq$5
Repeatability % (retention time)	0.75	-Lack of guidelines -Adopted $\leq$2
Accuracy % (single measurement)	−4.41	-Lack of guidelines -Adopted $\pm$10
Trueness % (average value from measurements)	−2.33	-Lack of guidelines -Adopted $\pm$5

Table 13
Parameters of validation and criteria acceptance for the quantitative analysis polydimethylsiloxane by SEC-ELSD.

Parameter of validation	Value	Criteria acceptance for pharmaceutical and chemical analysis		
Range (concentration %)	0.1–1.0	-Acceptable linearity, accuracy and repeatability; -For the assay of a drug substance or a finished (drug) product: normally from 80 to 120% of the test concentration		
Linearity	$y = 66.647\,x + 1.6844$ $R^2 = 0.9958$	Pharmacy Exhibits linearity $R^2 \geq 0.998$		Chemistry/environment Exhibits linearity $R^2 \geq 0.995$
Precision (%)		Pharmacy drug substance	Pharmacy drug products	Chemistry/environment
Concentration 0.3%	2.11	≤2	≤5	≤5
Concentration 0.5%	1.21	Pharmacy		Chemistry/environment
Concentration 0.8%	0.93	≤2		≤5
Repeatability R.S.D. (%)	1.42	Pharmacy ≤4		Chemistry/environment ≤15
Intermediate precision R.S.D. (%)	4.26	Pharmacy		Chemistry/environment
Recovery (%)/Trueness (%)	102.3	-Recovery at each level of 98–102 -±2		-Recovery at each level of 80–120 -±20
Limit of detection (concentration %)	0.03	-Compliance with identification criteria	-Typically acceptable signal-to-noise ratio 3.3:1	
Limit of quantification (concentration %)	0.08	-Compliance with identification criteria	-Typically acceptable signal-to-noise ratio 10:1	
Sensitivity (concentration %)	0.02	-Lack of guidelines		

value. For this reason the trueness of the method was also determined. For the determination of trueness the certified reference material (CRM) is necessary. However, there are no certified reference materials containing simeticone or dimeticone as an active pharmaceutical ingredient with excipients which are present in pharmaceutical preparations. Therefore, the recovery studies were performed. A sample of matrix from Manti Gastop tablets (Fig. 2b) with an exact amount (200 mg) of PDMS standard with a viscosity of 350 cSt was prepared. Three independent measurements were carried out for each extract of 3 separate matrix samples. Table 10 presents the values of the integrated peak areas, relative standard deviation (RSD) of these measurements (precision) and the percentage recovery (trueness).

The average recovery obtained for three independently samples was 102.32%, hence the trueness of the method was good with a relative error of +2.32%, particularly for complex matrix of the sample and procedure of preconcentration of the analyte. The repeatability for recovery test was 1.44% (Table 10). It should be noted that this result was similar to the result obtained for the quantitative analysis, with a value of 1.42% (Table 8).

3.3.4. Evaluation of the detection and quantification limits and sensitivity of the method

The detection and quantification limits and sensitivity of the method were determined from the standard deviation value of the integrated peak area measured for PDMS with a viscosity of 350 cSt and a concentration of 0.5% (Table 7). The sensitivity of the method was assessed as good for the reason that it was possible to detect differences between two concentrations of the standard solutions (i.e. when the signals were distinguishable by the detector). The results are shown in Table 11.

4. Conclusions

The results of this study showed that the size exclusion chromatography with evaporative light scattering detector (SEC-ELSD) method is suitable for identification of polydimethylsiloxanes presented in pharmaceutical formulations. The method is characterized by a high specificity. Depending on the degree of polymerization of PDMS, the various retention times and molecular weights were determined. It was verified that specificity is independent from the drug matrix or the various concentrations of PDMS. Irrespective of the field research (pharmacy, food industry, chemistry, environment), the main aim of validation is to establish the suitability of an analytical method for its intended use. The results obtained should be consistent with acceptance criteria differences in dependence of the area and the purpose of research. The acceptance criteria for pharmaceutical analysis are higher than these for other research field. For example, in pharmaceutical analysis the precision is ≤2% or ≤5%, depending on the type of the sample, while for bioanalysis the same analytical value is ≤15. Tables 12 and 13 showed the values of parameters of validation and acceptance criteria defined for the evaluation of usefulness of the SEC-ELSD method as a tool for speciation analysis of the polydimethylsiloxanes used in pharmaceutical industry, chemistry or environment.

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