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RESEARCH ARTICLE

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Determination of oleamide bulk-to-surface distribution in polypropylene for medical use depending on sterilization method and storage time

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Abstract

Oleamide is used as a lubricant in the manufacturing and application of polypropylene (PP) medical devices. Samples of PP were prepared with 0, 1500, and 15 000 ppm oleamide content as lubricant. The samples were either left non-sterile, sterilized with ethylene oxide (ETO), γ-radiation (γ) or autoclaved (A) and stored for up to 4 weeks. To determine the oleamide bulk-to-surface distribution depending on sterilization method and storage time an extraction method and a washing technique were applied. The oleamide content was determined by gas chromatography (GC-FID) and compared with the coefficient of friction (COF). The COF dependent on the measured lubricant content at the surface. The content of lubricant on the surface depends on the type of sterilization: ETO increased the lubricant content to some extent, γ-sterilization and autoclaving reduced it. After storage, no migration of the lubricant to the surface could be detected.

KEYWORDS

additives, chromatography, poly(propylene), radiation, surfaces

1 | INTRODUCTION

In the production of polymer compounds, lubricants are used for the modification of their processing- and application-related properties. Frequently used lubricants are oleamide and erucamide as representatives of the fatty acid amides as well as waxes, metallic stearates or fatty acid esters.[1,2] This study focuses on oleamide as a lubricant in a polypropylene (PP) compound for medical applications.

Besides its use as lubricant oleamide (*cis*-9-octadecenamide) is best known as a bioactive signaling molecule in animals under sleep deprivation.[3,4] Studies report pharmacological effects of oleamide such as anti-inflammatory and cannabinoid-like behavior, influence on specific receptors or even inhibition of human enzymes.[5,6] Widely used as lubricant with migratory properties in polymers it can leach from laboratory ware[7] and interfere with analytical studies[5] as well as from medical goods like syringes[8,9] and intravenous infusion bottles[6] and also from food and beverage packaging or baby bottles to enter the human body.[6] Currently, there are no regulations in the EU for the amount of leaching oleamides from medical devices or food packaging. Values measured so far are not classified as critical according to the present status.[6] Nevertheless, it should be the endeavor of manufacturers of

medical devices and packaging materials to keep the potential of leaching additives as low as possible.

Regarding their function, lubricants are on the one hand needed to ease polymer processing like extrusion and injection molding by reduction of friction.[2] On the other hand, they are needed to ensure product properties for example when the polymer parts need to slide over each other as in syringes[9] and bottles, bottle caps or closures for medical good or bottle caps for beverages.[10] Lubricants are in general incompatible with the polymer matrix provoking their migration from the polymer bulk to the surface.[2,11] The lubricant accumulates on the surface as intended and thereby reduces the coefficient of friction.[11,12] The speed and extent of the migration of the lubricants depend on various parameters, for example, the nature of the lubricant and the polymer as well as their interaction, in particular defined via the difference of their surface energies.[11] Slower migration is observed in semi-crystalline polymers than in amorphous polymers. Oleamides are generally considered to migrate faster than erucamides.[2] In addition, a dependence on storage conditions such as temperature and duration can be observed, while migration is generally enhanced with both parameters.[11,13,14] Taken together with the minimization of leaching, an optimal polymer compound composition ensures simple polymer processing as well as required sliding material properties while avoiding excessive accumulation of the lubricant on the surface.

As consequence, a basic understanding of the migrating properties within the complete process chain, ranging for medical applications from, for example, injection molding through various sterilization methods to storage, must be established.

Within this context, we investigated the migration of oleamide in PP in function of time and concentration after application of the three following sterilization methods. Ethylenoxide (ETO) sterilization is a common method used in the industry to sterilize polymers. In the process, heat and radiolytic stress are avoided. Due to the use of the potential hazardous gas, ETO, the process is strictly controlled and the possibility that the polymer can absorb the gas must be considered.[15,16] Also widely used is radiation sterilization (here used γ-radiation). When sterilizing polymers with radiation changes in the molecular structure can occur. In the presence of oxygen this can lead to oxidation,[17] resulting in decomposition of the main chain, bond scission and/or cross-linking.[15,16,18,19] Autoclaving, which was also investigated as an example for a heat treatment, can result in thermal degradation of polymers, resulting in oxidation and hydrolysis.[16] Therefore, it is not a large-scale industrial procedure for polymers but widely used in medical practices and a possible way to perform sterilization of medical devices in crisis areas without sufficient supply of disposable products. Although it is well known that different sterilization methods have different influences on polymers like reducing their mechanical properties, yellowing, chain scission and/or crosslinking and degradation,[17,20,21] no literature could be found on the comparison of the specific influence of these sterilization methods on the migrating properties of the lubricant oleamide in polypropylene.

The coefficient of friction was determined by means of a tribometer and correlated to the lubricant content. The content of oleamides in polymers can be determined via extraction, for example, with solvents,[22–25] and subsequent analysis, for example, chromatographic methods,[25–28] both gas and liquid chromatography, or by means of FTIR spectroscopy.[10,29] In the present study, the extraction of lubricant from surface and bulk material was performed prior and after sterilization and storage by ultrasonic extraction in dichloromethane followed by GC-FID measurement. Furthermore, a simple washing technique via dipping samples for a short period in dichloromethane was investigated as indicator for surface near lubricant concentrations. The lubricant was identified by GC–MS analysis as well as by FTIR.

With regard to the study design following hypothesis are stated: (i) after storage more lubricant is found in the surface layer than in the bulk, (ii) after autoclaving and ETO sterilization more lubricant is found in the surface layer than in the bulk due to migration caused by increased temperature, after γ-sterilization the lubricant content on the surface is expected to remain constant, (iii) the extraction of the surface layer and the washing method performed give similar trends with regard to the lubricant migration, and (iv) the COF corresponds to the surface near lubricant content.

2 | EXPERIMENTAL

2.1 | Materials, specimen preparation, and study design

Three series of polymer compounds based on the PP random copolymer (Purell RP-type for medical/pharmaceutical application, lyondellbasell, Rotterdam, Netherlands) were used: pure without the addition of oleamide, with 1500 ppm oleamide and with 15 000 ppm oleamide (Crodamide OR-MB-[GB], Croda, Gouda, Netherlands). To compound and granulate the material the extruder ZE25 × 32 D (Berstorff, KrausMaffei GmbH, Hannover, Germany) and the granulator SGS50 E (Scheer, MAAG, Oberglatt, Swiss) were used. Injection molding of square samples (30 × 30 × 4 mm) in a polished stainless steel form was conducted with the Babyplast (Christmann, Kierspe, Germany) under following conditions: 190°C, 34 bar, 27.9 s cycle time, 20.1 s cooling time, 3 s post-printing time.

Twenty-seven specimens without oleamide and 54 specimens with 1500 and 15 000 ppm oleamide, respectively were prepared. After processing, the samples were stored at room temperature and only touched by glove. No intentional contamination was applied to the samples. The samples were tested (coefficient of friction and quantification of oleamide) immediately after production, after 1 week of storage (non-sterile), respectively after sterilization (due to shipment sterilization samples returned 1 week after production), and after another 3 weeks of storage. The coefficient of friction measurement was performed on the same samples used for the extraction method before surface layer separation by the microtome. The quantification of oleamide in surface layers and the bulk material was performed using an extraction method ($n = 3$ for each sterilization method and storage time) as well as a washing method ($n = 3$ for each sterilization method and storage time) to determine the oleamide content on the sample surface as additional method.

2.2 | Sterilization methods and storage

Each sterilization method was performed on 30 samples (6 samples—0 ppm; 12 samples—1500 ppm; 12 samples—15 000 ppm). Due to the shipping time for ETO- and γ-sterilization, there was 1 week delay between the production of the samples and the tests. During the ETO sterilization the samples were exposed to ethylenoxide for 1 h. The maximum chamber temperature was 55°C. The γ-sterilization was performed at BGS Beta-Gamma-Service GmbH & Co. KG (Wiehl, Germany). A radiation dose between 25 and 30 kGy with a dose rate of 8 kGy/h was targeted. The measured radiation dose was 29.08 kGy. To aim for a comparable temporal context, autoclaving was performed 1 week after production of the samples using the Autoklav 15 (MELAG Medizintechnik GmbH & Co. KG, Berlin, Germany) at 134°C and 2 bar for 5 min. The autoclaving method used is considered a worst-case scenario, as these settings can have a significant impact on the polymer, when not heat stabilized,[16] and thus likely on the additivation.

The storage of the samples took place at room temperature. The maximum storage period was 3 weeks after the return of the samples from sterilization and thus a maximum of 4 weeks after production.

2.3 | Coefficient of friction determination

Coefficient of friction (COF) was measured on the square surface (30 × 30 mm) of the samples against a steel ball (diameter of 6 mm) with the tribometer TRB and Software InstrumX Version 7.3.17 (Anton Paar OptoTec GmbH, Seelze, Germany). The measurement was performed with $n = 3$ in rotation mode (one rotation) in a diameter of 10 mm at a contact pressure of 5 N and a velocity of 0.05 cm/s. The dimensionless COF (μ) is calculated from the frictional force (F_f) divided by the normal force (F_n) with $\mu = F_f/F_n$.[30]

2.4 | Extraction, qualification, and quantification of oleamide

To determine the bulk-to-surface distribution of oleamide an ultrasonic extraction method was performed for each sample series, sterilization method and point of time on three samples ($n = 3$). Prior to extraction of the oleamide, the four lateral surfaces of the samples (4 × 30 mm) were removed in sections of 30 μm each using a microtome (Jung RM2065, Leica Mikrosysteme Vertrieb GmbH, Wetzlar, Germany) until in sum a target weight of ~36 mg was reached. For sample removal of the bulk material, the surface (30 × 30 mm) was abraded with 180 grit sandpaper. Cuts were made to reach the bulk (1.5 mm distance from the last surface layer) and then again 30 μm thick layers were removed for in sum a target weight of ~36 mg. The oleamide was extracted from these pooled surface and bulk layers with 4 ml dichloromethane (GC grade, Carl Roth GmbH, Karlsruhe, Germany) in closed glass vials for 90 min in an ultrasonic bath (Elmasonic S 60 H, Elma Schmidbauer GmbH, Singen, Germany).

In addition to this extraction method, a washing method was performed on three samples of each sample series. For this purpose, the entire sample was placed in 8 ml dichloromethane in the ultrasonic bath for 5 min. The extract was transferred to 10 ml glass flasks and refilled to 10 ml with dichloromethane.

To quantify the amount of oleamide extracted, a gas chromatograph with flame ionization detector (GC-FID) (Clarus 690, PerkinElmer, Waltham, MA) was used and operated with the carrier gas helium. Samples and calibration solutions were measured in duplicate. The GC-FID method used was applied as a modification of the method of Farajzadeh et al.[25] A liquid injection volume of 3 μl was injected to a 220°C heated split injector. The split ratio of the gas phase was set at 10:1 with a gas flow of 1.5 ml/min. The GC was equipped with an Elite 5 MS column (30 m, ID 0.25 mm, 0.25 μm). The temperature program started at 150°C and was held for 3 min. The temperature was increased to 220°C at a rate of 30°C/min. This final temperature was held for 11 min. The chromatogram was detected using a flame

ionization detector, which was set to 320°C. Synthetic air and hydrogen were used as fuel gases. The duration for the measurement of one injection was 16.3 min. The calibration of oleamide was based on the largest peak at a retention time of about 13.6 min. Dichloromethane was used as solvent for preparing the calibration solutions. For quantification, a linear calibration curve was constructed over six calibration points in the concentration range of 0.5–50 mg/L on each measuring day. Detection and quantitation limits were specifically recalculated for each measurement day and were 0.53 and 2.16 mg/L, respectively, as a minimum. To qualify the oleamide peak at a retention time of about 13.6 min, the gas chromatograph was coupled with the mass spectrometer (SQ8, PerkinElmer, Waltham, MA) which worked in TIC mode with m/z 30–600. The chromatographic method was the same as described previously and an identical column was used.

In addition, the lubricant was identified by Fourier transform infrared spectroscopy with attenuated total reflection (ATR-FTIR) on the sample surface before and after sterilization. ATR-FTIR measurements were carried out with a NICOLET iS20 (Thermo Fisher Scientific GmbH, Dreieich, Germany) with ATR attachment Smart Endurance (Thermo Fisher Scientific GmbH) and evaluated with the OMNIC 9.9 (Thermo Fisher Scientific GmbH) software.

2.5 | Statistical analysis

Statistical analysis was conducted with the statistic software Prism (GraphPad). Significant differences between the mean values were determined using a one-way analysis of variance (ANOVA) with significance level $\leq .05$ (Tukey test). Normal distribution was tested with the Shapiro–Wilk test, variance homogeneity was tested with the Barlett's test.

If the requirements of ANOVA were not met, significant differences between values were determined using a Kruskal-Wallis test with significance level $\leq .05$. This was the case for the data sets surface A—1 week, surface ns—4 week, surface γ—4 week, bulk A—4 week, and bulk ETO—4 week with 1500 ppm oleamide from the extraction method; for the data sets surface γ—1 week, surface A—1 week, surface A—4 week, surface ETO—4 week, bulk γ—4 week and bulk ETO—1 week with 15 000 ppm oleamide from the extraction method; for the data set ETO—1 w with 1500 ppm oleamide from the washing method; for all data sets with 15 000 ppm oleamide from the washing method and for all data sets from the COF measurement.

3 | RESULTS AND DISCUSSION

3.1 | Coefficient of friction depending on sterilization method and storage time

COF was considered as a factor to prove the effectiveness of the oleamide. This is shown as an average value for the sample series without lubricant (0 ppm) and for the sample series with oleamide (1500 and 15 000 ppm) for the different sterilization types and storage times in Figure 1A. It can be seen that the COF was significantly reduced by the addition of lubricant. This reduction was already achieved with an addition of 1500 ppm lubricant. Increasing the lubricant content to 15 000 ppm did not lead to any further significant reduction of the COF in most cases. The measured values of COF for the sample series without oleamide (0 ppm) appeared independent on sterilization method and storage time. For the samples with 1500 ppm lubricant content, the COF after γ-sterilization reduced only slightly compared with the samples without lubricant content. At a content of 15 000 ppm, this effect was not observed; here, a similarly low COF was measured as for the non-sterile samples. A similar trend, although less pronounced, was observed for the autoclaved (A) samples. Here, too, a significant difference could be seen in the samples with 1500 ppm lubricant content compared with the non-sterile samples with the same lubricant content. There was no effect of the 4-week storage period on the measured COF.

3.2 | Oleamide content on sample surface depending on sterilization method and storage time

The lubricant could be identified by ATR-FTIR measurement on the samples surface before and after sterilization. Figure 2 shows the FTIR spectra for a sample without lubricant (ns—0 ppm), the pure oleamide and exemplarily of an autoclaved sample with the initial content of 15 000 ppm lubricant (A—15 000 ppm). The bands of N-H stretching at 3184 and 3375 cm^{-1} as well as those of C=O stretching at 1631 and 1657 cm^{-1} of the amide can be seen particularly well. Quantification of the oleamide content on the specimens was not possible due to the overlap of the bands of PP and oleamides, since no non-changing band was available as a reference for normalization.

Qualitative as well as quantitative determination of oleamide by gas chromatography proved to be effective. The eluting substance at 13.6 min was confirmed by GC–MS as oleamide. To measure the oleamide content

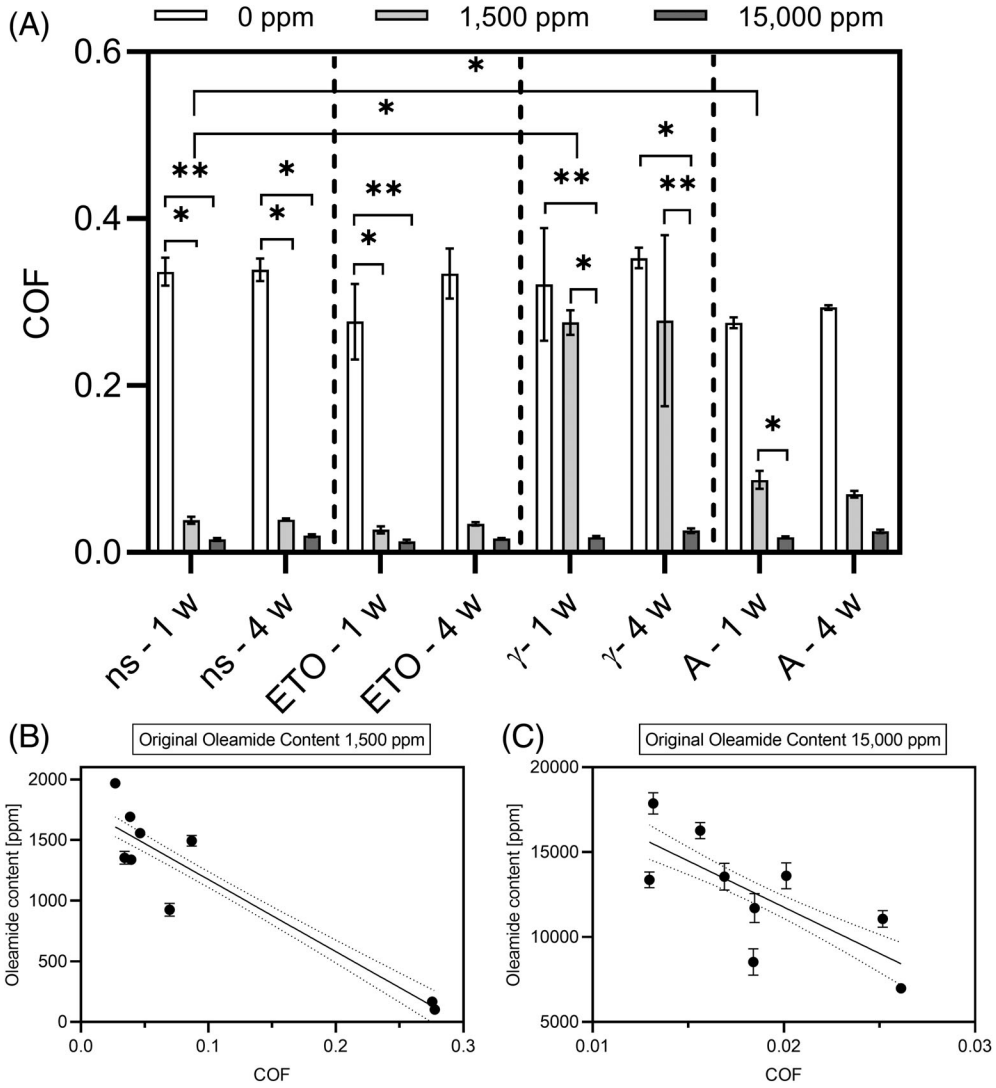

FIGURE 1 (A) COF for the sample series 0, 1500, and 15 000 ppm for non-sterile samples, all sterilization methods and storage times; (B) Oleamide content [ppm] of all sample surfaces (extract) from the 1500 ppm series as a function of COF shown as a linear regression with a confidence interval of 95% and (C) Oleamide content (ppm) of all sample surfaces (extract) from the 15 000 ppm series as a function of COF shown as a linear regression with a confidence interval of 95%. Statistically significant differences are marked with * ≥ .05, ** ≥ .01, and *** ≥ .001 ($n = 3$). ns, non-sterile; ETO, after ETO sterilization; γ, after γ-sterilization and A, after autoclaving

on the surface of the specimens two different techniques were used. On the one hand, the surface layers were cut from the specimens and the oleamide was extracted by the solvent. On the other hand, a washing technique was used, where the lubricant was washed from the surface with the solvent. Ultrasonic extraction with dichloromethane thus proved to be effective. Similar extraction methods have already been described by Nielson et al.,[22] who extracted additives from polypropylene and polyethylene with mixtures of dichloromethane and further solvents.

Figure 3 shows the measured lubricant contents of the sample surfaces of the two methods (extraction and washing technique) used for the different lubricant contents (1500 and 15 000 ppm) of the differently sterilized samples (ethylene oxide (ETO), gamma radiation (γ), autoclave (A), at the two storage time points of 1 and 4 weeks). The mean lubricant content of the sample series were normalized to the samples in the initial state (non-sterile samples directly after production [ns—0 week = 100%]). The measured data are shown in Table 1 A and B.

The extraction method shows similar trends for the 1500 ppm (a) and 15 000 ppm (b) lubricant sample series. The non-sterilized samples appeared to exhibit significantly lower surface lubricant content with increasing storage time. Surface lubricant content increased significantly in samples sterilized with ethylene oxide (ETO—1 week), but the effect did not persist over a 4-week period (ETO—4 week). A strong pronounced influence could be seen through γ-sterilization. Here, significantly less lubricant was measured on the sample surface after both 1 and 4 weeks. Likewise, a measurable reduction occurred after autoclaving. The latter was more pronounced for the samples with 15 000 ppm lubricant content than for the samples with 1500 ppm lubricant content. In general, there was a tendency for the lubricant contents after extraction to show less lubricant on the sample surface after 4 weeks of storage than after 1 week of storage. This effect was less pronounced when

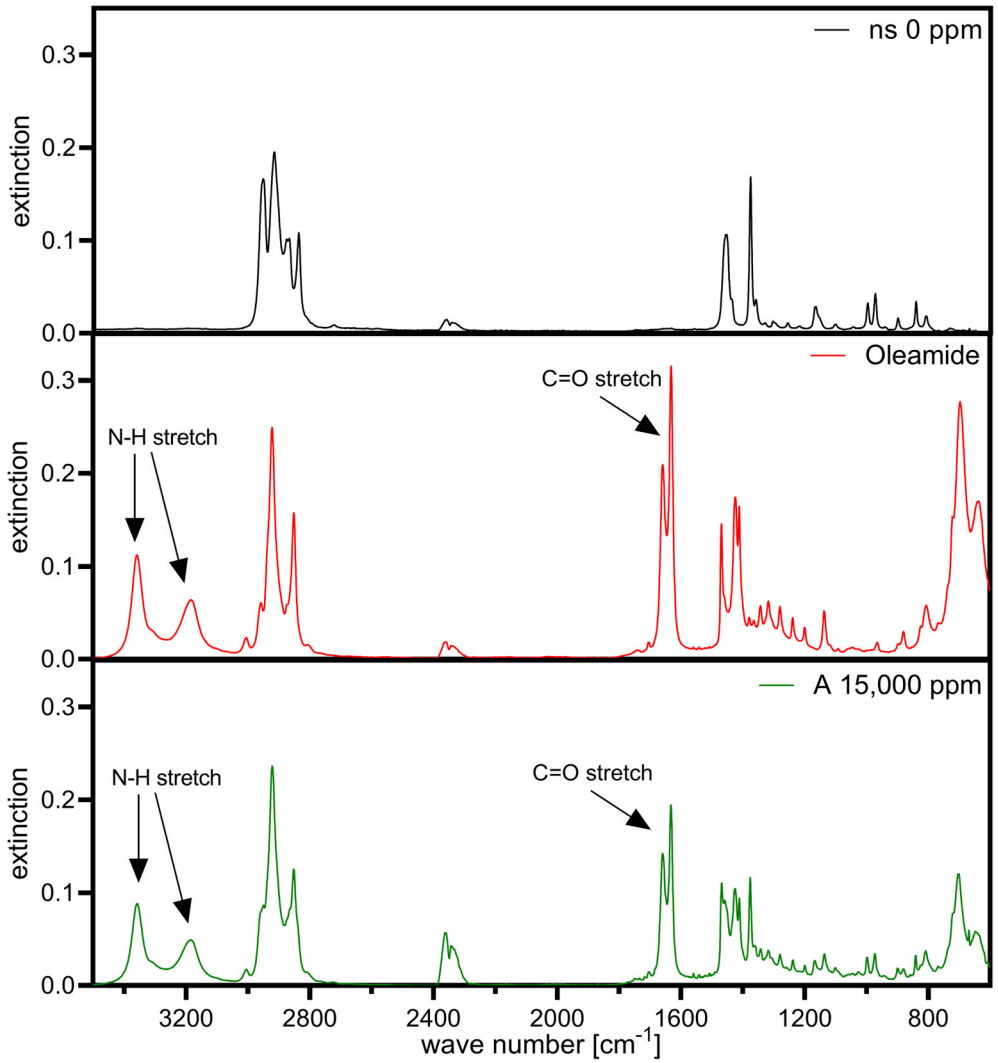

FIGURE 2 ATR-FTIR spectra of pure PP without oleamide (ns 0 ppm—black), pure oleamide—red and a specimen after autoclaving with initially 15 000 ppm oleamide—green. The stretching of the N—H and C=O bonds of the amide are marked with arrows

the washing technique was used (Figure 3C,D). Here, the reduction only occurred in the sample series ETO and A of the samples with 1500 ppm lubricant content. As with the extraction method, an increase in the lubricant content on the surface of the samples sterilized with ethylene oxide could also be measured with the washing technique. With this method, the influence of γ-sterilization was more evident for the samples with 1500 ppm lubricant content. The GC-FID method used did not yield a quantifiable lubricant content for this series of samples. For the samples with 15 000 ppm lubricant content, there was also a strong reduction of the lubricant content on the sample surface after γ-sterilization. Regarding the trend in autoclaved samples, the washing technique differed from the extraction method. An increase in the lubricant content on the sample surface was measured after 1 week of storage for the samples with 1500 ppm lubricant content. However, this was followed by a reduction after 4 weeks of storage.

Comparing the results of the washing technique with those of the extraction method, differences could be observed with regard to the measured lubricant contents on the sample surfaces depending on the storage time (Figure 3). However, the general trend of the influence of the sterilization methods used was clear for both methods. In particular, a difference was evident in the results of the samples with an addition of 1500 ppm lubricant after γ-sterilization. In the extraction method, lubricant was detectable in small amounts. With the washing technique, no lubricant could be quantified and did not exceed the detection limit of 0.53 mg/L for some samples. This indicates that the washing technique can be judged as more surface sensitive. In the sections for the extraction method, a total of ∼90 μm thick layers were removed on each surface in order to exceed the reliably detectable lubricant concentrations required for the GC-FID method after extraction in the solution. This layer thickness was defined as near the surface, but it is possible that the measurements are already influenced by effects from the bulk. Furthermore, the washing technique proved to be quickly feasible. The dichloromethane of the entire sample surface could be

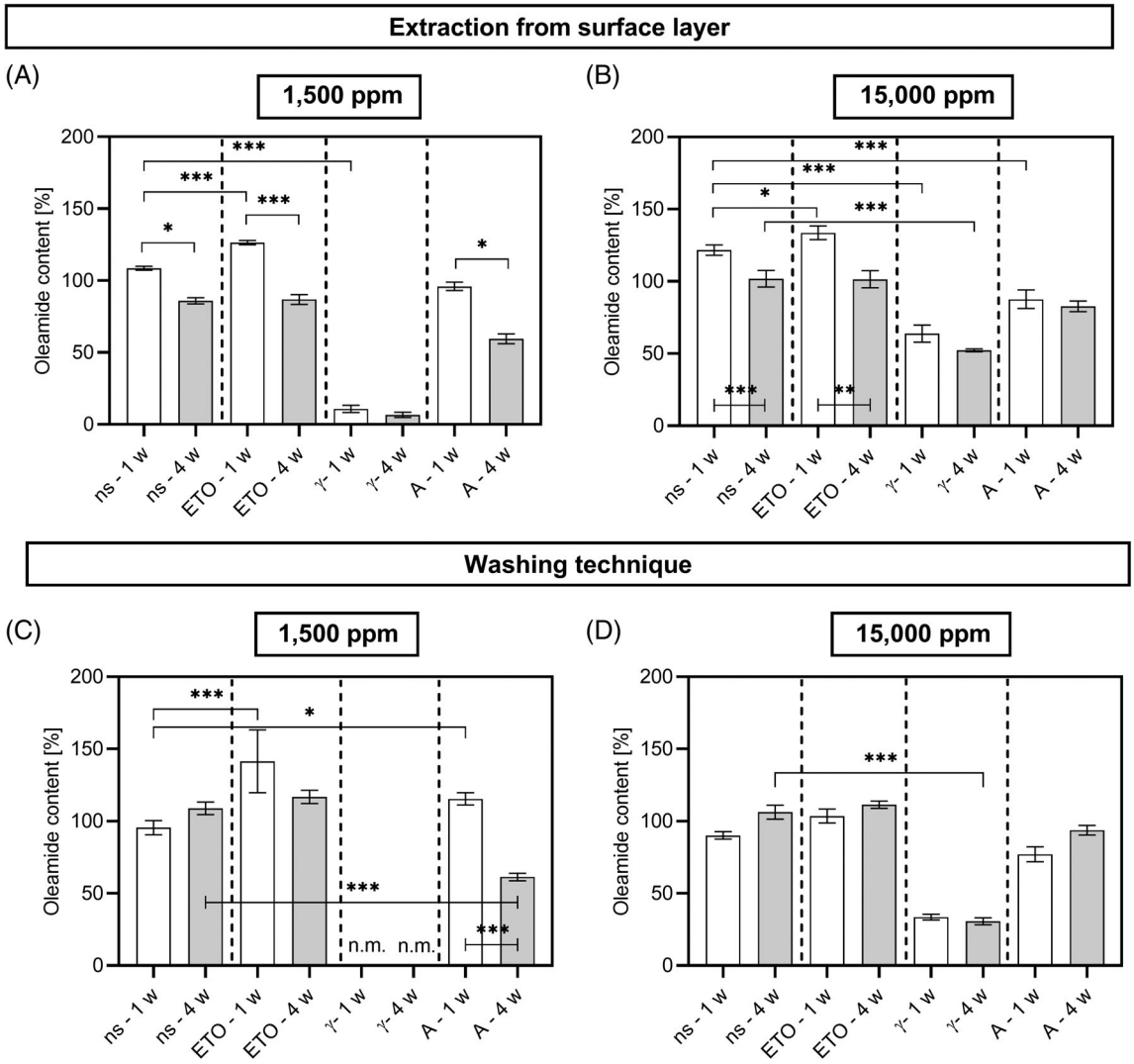

FIGURE 3 (A) Mean oleamide content (%) ± *SD* in the surface after extraction from sample series 1500 ppm, (B) In the surface after extraction from sample series 15 000 ppm, (C) Measured with the washing technique of the sample series 15 000 ppm, and (D) Measured with the washing technique of the sample series 15 000 ppm. Statistically significant differences are marked with * ≥ .05, ** ≥ .01, and *** ≥ .001 ($n = 3$). ns, non-sterile; ETO, after ETO sterilization; γ, after γ- sterilization, and A, after autoclaving

taken into account, whereas with the extraction method only the side surfaces (4 × 30 mm area) of the samples were available for sampling. On the other hand, the samples used for the extraction could be assigned one-to-one to the values of the measured COF, since this was done on the same samples (30 × 30 mm surface) (Figure 1).

3.3 | Bulk-to-surface distribution of oleamide depending on sterilization method and storage time

To determine differences between the lubricant content at the surface and in the bulk of the specimens, samples were taken from corresponding areas and analyzed. Figure 4 shows the measured lubricant contents at the surface and in the bulk for the specimens with 1500 ppm (A) and 15 000 ppm (B) lubricant content. The measured values are normalized to the samples in the initial state (non-sterile samples directly after production [ns—0 week = 100%]). The measured data is shown in Table 1 A and C.

As a trend across all measurements presented here, it appears that the measured lubricant content in the bulk was at least similar to or higher than that at the surface of the samples. After 4 weeks of storage, there was a tendency toward lower lubricant values both in the bulk and at the surface.

The comparison of the lubricant content in the bulk material and on the sample surface was set up to check the influence of the sterilization methods and to observe possible shifts in the concentrations during storage. The sterilization methods had the effect on the lubricant

TABLE 1 Measured oleamide content (ppm) or (μm) and oleamide content (%) normalized to the samples initial state (non-sterile samples directly after production (ns—0 week)) after A: Extraction from the surface layer, B: Application of the washing technique and C: Extraction from the bulk

A: Extraction from surface layer				
	Aimed oleamide content: 1500 ppm		**Aimed oleamide content: 15 000 ppm**	
Sample series	**Oleamide content (ppm)**	**Oleamide content (%)**	**Oleamide content (ppm)**	**Oleamide content (%)**
ns—0 week	1557	100	13 365	100
ns—1 week	1691	109	16 268	122
ns—4 week	1338	86	13 610	102
ETO—1 week	1968	126	17 863	134
ETO—4 week	1353	87	13 561	102
γ—1 week	167	11	8535	64
γ—4 week	102	7	6979	52
A—1 week	1494	96	11 708	88
A—4 week	926	60	11 065	83
B: Washing technique				
	Aimed oleamide content: 1500 ppm		**Aimed oleamide content: 15 000 ppm**	
Sample series	**Oleamide content (μg)**	**Oleamide content (%)**	**Oleamide content (μg)**	**Oleamide content (%)**
ns—0 week	111	100	995	100
ns—1 week	106	96	897	90
ns—4 week	121	109	1058	106
ETO—1 week	158	142	1031	104
ETO—4 week	130	117	1109	111
γ—1 week	-	-	334	34
γ—4 week	-	-	305	31
A—1 week	129	115	767	77
A—4 week	68	61	934	94
C: Extraction from bulk				
	Aimed oleamide content: 1500 ppm		**Aimed oleamide content: 15 000 ppm**	
Sample series	**Oleamide content (ppm)**	**Oleamide content (%)**	**Oleamide content (ppm)**	**Oleamide content (%)**
ns—0 week	1554	100	12 527	100
ns—1 week	1860	120	16 744	134
ns—4 week	1602	103	14 768	118
ETO—1 week	1942	125	16 519	132
ETO—4 week	1675	108	14 158	113
γ—1 week	1420	91	13 409	107
γ—4 week	1153	74	13 081	104
A—1 week	1827	118	13 004	104
A—4 week	1500	97	13 368	107

Note: Data are visualized in Figures 3 and 4.

content on the sample surface as described above. However, the effects were limited to this area and did not reach the bulk material. This is particularly clear for the values measured after γ-sterilization. In general, it was expected that if the lubricant content at the sample surface is reduced after sterilization, this will rebalance over the evaluated storage time due to migration processes; this means it was expected that the surface lubricant

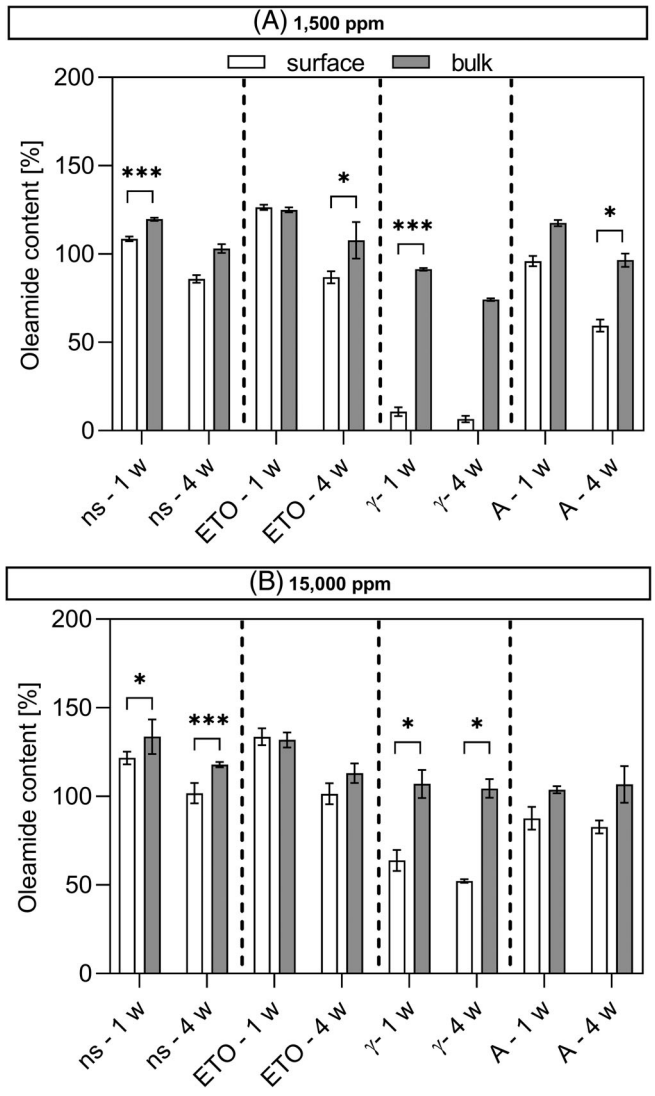

FIGURE 4 Oleamide content (%) ± *SD* in the surface and bulk after extraction from (A) Sample series 1500 ppm and (B) Sample series 15 000 ppm. Statistically significant differences are marked with * ≥ .05, ** ≥ .01 and *** ≥ .001 ($n = 3$). ns, non-sterile; ETO, after ETO sterilization; γ, after γ-sterilization; and A, after autoclaving

content will increase with storage time. However, this did not apply to the present results. This contrasts with the observations of Joshi et al.[31] They observed by means of Fourier transformation infrared microspectroscopy the distribution of erucamides in LLDPE films directly after preparation and after aging (60°C, 4.5 h). The previously uniformly distributed lubricant was accumulated on the sample surface after aging (about 40% of the lubricant). Furthermore migration of behenamide and erucamide to the surface of highly crystalline HDPE caps were observed by Dulal et al.[10] after 14 days of aging (temperature not given) by using GC-FID measurements. This leads to the consumption whether the chosen storage period was too short or the storage temperature (room temperature) too low to see an effect.

3.4 | Correlation of COF and oleamide content

Figure 1B,C show the measured lubricant contents (ppm) from the extracted sample surface as a function of the measured COF. Both measurements were performed on the same samples and can therefore be directly compared. For the samples with an addition of 1500 ppm lubricant (B) as well as for the samples with 15 000 ppm lubricant (C) a roughly linear dependence between the measured lubricant content of the sample surface and the COF could be drawn. However, in order to prove a clear dependence, further tests with defined lubricant contents would have to be compared with the respective COF. Dependencies of the COF on the lubricant content on the sample surface have already been reported in literature.[32,33] Although these studies refer to erucamide as a lubricant, similar behavior is assumed for oleamide, which was observed in the current study. Ramirez et al.[34] observed a relationship between the surface concentration of erucamide and the COF of linear low-density polyethylene (LLDPE) films. They reported a plateau of the COF kinetic at erucamide surface concentrations above ~0.5 μg/cm^2. A similar trend with the formation of a plateau of the COF would also be conceivable in the current study. The COF values of the samples with an initial lubricant content of 15 000 ppm all showed quite similar values to each other. It would be interesting to take a closer look at the dependence of the COF for the range between 1500 and 15 000 ppm oleamide content. However, from the present results, it can be concluded that an addition of 1500 ppm oleamide is sufficient to significantly reduce COF. According to the present findings, an addition of 15 000 ppm would only be significant for a targeted sterilization with γ-radiation. This statement is of course dependent on the desired COF in the use of the product.

The conclusion that γ-sterilization has a clear influence on the lubricant content on the sample surface can be stated (Figure 3 and 4). This was more pronounced for the samples with 1500 ppm lubricant content. It can be assumed that the radiation sterilization damages or even erodes the molecules of the oleamide, as chain scission and oxidation is a documented phenomenon of γ-sterilization for polymers.[20] Since the observed COF after γ-sterilization is comparable to the one of non-sterilized samples (Figure 1A), the lubricant seems to be either no longer present on the surface or no longer present in its original molecular structure. In literature this effect was also seen by Demertzis et al.,[35] who found erucamide to degrade in LDPE and PP after γ-radiation with 44 kGy. They also were not able to detect the resulting degradation products by GC/MS analysis. Celiz et al.[36] observed the leaching of erucamide from PE after γ-sterilization with doses between

0.5 and 20 kGy. Reduced leaching of erucamide was observed at 20 kGy, no changes were observed <20 kGy. Wang et al.[37] came to a similar finding with 10 kGy doses of γ-radiation on PET/PE films, where leaching of erucamide was not different between treated and untreated samples. From these results, it could be concluded that oleamide degradation occurs at the 29 kGy dose used. At lower radiation doses, it would be possible that this degradation does not occur. A limitation to be mentioned here is that the polypropylene used was a non-radiation-stabilized polymer. Likewise, effects from the reaction of the polymer with the γ-radiation could also be involved here. If this was the case, however, an increased COF would have also appeared in the samples with 15 000 ppm lubricant after sterilization, but this could not be seen. For the samples with 15 000 ppm lubricant, the effect was generally less pronounced. Although a reduced amount of lubricant was measured on the sample surface (Figure 3 and 4), this did not seem to have an effect on the COF. It could be possible that there was already so much lubricant in several layers on the sample surface that a reduction of the lubricant fraction by the γ-radiation only affects a part of the lubricant. Thus, after sterilization, there would still be enough lubricant to keep the COF low. Conflicting effects were measured for the autoclaving sterilization process. For the extraction method, a significant reduction of the lubricant content at the surface was measured for the samples with 15 000 ppm, whereas for the washing technique, a significant increase of the lubricant content was found for the samples with 1500 ppm (Figure 3). If these results are compared with the measured COF (Figure 1A), this confirms the measurements of the washing technique. The COF for this series of samples was significantly decreased compared with the non-sterile samples (after 1 week of storage). For the samples with 15 000 ppm oleamide, again no effect on the COF could be seen. After sterilization with ethylene oxide, increased lubricant levels are measured on the specimen surfaces, except for the washing technique applied to the specimens with 15 000 ppm lubricant content (Figure 3). However, this increased amount of lubricant on the surface did not lead to lower COF values (Figure 1A).

4 | CONCLUSION

The concentration of the lubricant content at the surface as well as in the bulk of the samples was measured as a function of sterilization and storage time and compared with the COF. The COF depends on the measured lubricant content at the surface. Both the extraction method and the washing technique used were found to be applicable. The content of lubricant on the surface depends on the type of sterilization. While sterilization with ethylene oxide increased the lubricant content to some extent, it was reduced by γ-sterilization and autoclaving. Thus, sterilization with ETO shows the least influence and is preferable to the other two methods when using oleamides in PP. Should one of the other methods be used, prior studies on the effect on slip properties for the specific application are required. After storage, less lubricant was found in the area near the surface than in the bulk, thus no migration of the lubricant to the surface could be detected. The findings and methods can be transferred to medical products made of PP, which represent a sliding system, such as syringes or closure caps.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in the publication of this article.

AUTHORS CONTRIBUTORS

Eva Berghaus did the conceptualization of the study, developed and validated the methodology used. She also did the investigations, formal analysis and visualization of the data and writing the original draft. Hendrik Ruppel and Lara-Sophie Martin developed the methodology, did investigations, reviewed, and edited the writing. As supervisor and project administrator Svea Petersen helped with the conceptualization of the study, reviewed, and edited the writing. All authors have approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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