Influence of Processing Conditions on the Leaching of Thermal Stabilizers from Plasticized Polyvinyl Chloride in the Presence of Water

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ABSTRACT: Plasticized PVC formulations for pharmaceutical packaging contain calcium and zinc stearates, which are PVC heat stabilizers. It was found in the literature that these additives can migrate to some aqueous solutions, especially when the pH is alkaline, the best example being sodium bicarbonate solutions. So, the aim of this work was to demonstrate the correlation between the lubricant ability of these stearates and their further migration in fluids. For this purpose, we studied the migration of calcium and zinc stearates during an extrusion step, focusing essentially on slip phenomenon. We have demonstrated here that slip phenomenon occurs in the case of plasticized PVC heat stabilized by calcium and zinc stearates. The slip phenomenon amplitude increases with the total amount of stearates in the formulation and also when the extrusion temperature decreases. The analysis of a die insert through scanning electron microscopy coupled with an X-ray energy dispersive technique could allow us to see that the additive mainly responsible for the slip is calcium stearate. The analysis of the leachable components of the formulations migrating after steam sterilization in sodium bicarbonate solutions leads to conclude that zinc stearate also migrates to the metal surface of the die during extrusion, but in a lower extent than calcium stearate. So, a good correlation exists between the processing conditions, including essentially the stearate concentration and the extrusion temperature, and the migration of these additives from the extruded sample to aqueous solutions. © 1998 John Wiley & Sons, Inc. J Appl Polym Sci 70: 2391-2400, 1998

Key words: leaching; plasticized polyvinyl chloride; water

INTRODUCTION

Plasticized polyvinyl chloride (PVC) formulations are widely used as primary packaging materials for blood and infusion fluids. The plastic materials may contain up to 45% of additives.¹ The need for additives during the processing of PVC arises mainly from the inherently poor thermal stability of PVC in the processing temperature range. The function of lubricant in plasticized PVC is to reduce friction on surfaces, including the reduction of adhesion between the polymer melt and the metal surfaces of the processing equipment.

However, a possible interaction between the container and the content is the migration of such components from the plasticized PVC. Usually the migration of leachables onto the surface of PVC is slow, but it seems that the sterilization process may encourage the migration faster, and the thickness of leachable components may be affected by the sterilization type.²

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Zinc and calcium salts of stearic acid are used primarily as thermal stabilizers in flexible PVC formulations where a low toxic hazard is required. Nevertheless, stearates have also been identified in intravenous solutions.^{3,4} G. Smistad et al.³ showed that the concentration of stearates greatly increases with the PH of the solution. In the case of sodium bicarbonate where the pH ranges from 7 to 8.5, the concentration of stearates is so high that these stabilizers have to be replaced.⁵ Furthermore, it is known that stearates can act as lubricants in plasticized PVC formulations, but there are few reports concerning the influence of processing conditions on the migration of stearates towards the surface.^{6,7} This article discusses the influence of the processing conditions on the migration of zinc and calcium stearates from plasticized PVC to the PVC/metal interface. Actually, slip phenomenon of the PVC melt at the metal interface is investigated. A correlation between processing conditions and migration of zinc and calcium stearates in sodium bicarbonate solutions is attempted.

EXPERIMENTAL

Materials

A suspension PVC (Solvic 271 GA) supplied by Solvay, was used. The plasticizer (Garbeflex DOP D40), a diethylhexyl phatalate supplied by CECA, was used at a ratio of 40 weight parts per hundred weight parts of PVC (phr). The heat stabilizer was a mixture of calcium and zinc stearates. Stavinor Cecavon CA and Stavinor Cecavon ZN from CECA. The total amount of stearates varies from 0.15 to 0.84 phr, and the molar Ca/Zn ratio is kept constant at 1.7. An epoxydized soya oil (Ecepox PB3 from CECA) was added at a ratio of 6 phr.

Extrusion Experiments

The different PVC formulations were extruded with a counterrotating twin-screw extruder (Leiztritz LSM 30-34, centerline distance C1 = 30 mm, screw diameter: D = 34 mm, length-to-diameter ratio L/D = 16). The extruder barrel is divided into six equal zones. Each zone has individual electrical resistance heaters and a water cooling system for controlling the self-heating of the melt polymer due to the viscous dissipation phenomenon. For all experiments, the screw rotation



Figure 1 Geometry of the slit rheometer. Location of the pressure transducers (P2, P3, and P4) and location of the infrared temperature transducer.

speed of the extruder was fixed at 40 rpm and the flow rate at 3 kg/h.

Slit Rheometer

The extruder was equiped with a slit rheometer, as shown in Figure 1, where the position of thermal and pressure transducers (Dynisco PT 482) can be seen. The dimensions of the slit die are 50 \times 50 \times 2 mm³. The pressure sensors (P2, P3, and P4) allow us to determine the gradient pressure inside the die, and the thermal sensor gives the bulk temperature. The wall shear stress τ_w was calculated from the steady-pressure gradient *p*:

$$\tau_w = \frac{p \cdot h}{2} \tag{1}$$

It should be noticed that the melt temperature is one of the most important parameter. Because of the problems to measure the true temperature during extrusion with classical temperature measurement devices, like thermocouples, a method based on infrared radiation was previously developed.⁸ The infrared sensor measures the mean bulk's temperature in the cone volume in front of the window of the sensor. Furthermore, the measurement with an infrared temperature sensor can be assumed to be instantaneous (in the milliseconds order of magnitude).

Dies with two different surface states were used: (1) a rough surface obtained by electroero-

sion; and (2) a polished surface obtained after different steps of polishing ranging from 15 to 3 μ m. These dies were cleaned inside an oven at 600°C for several hours and then removed from the dust with compressed air for the first one, and with a 3- μ m polishing solution for the polished one.

As the flow rate in the extruder was fixed at 3 kg/h, the corresponding apparent wall shear rate, which was, therefore, constant for the whole study, was 15 s⁻¹.

Metal Surface Analysis

As the die was too large to be mounted on the microscope sample holder, an apparatus was conceived⁹ to put the surface of a small metallic sample of the same steel as the die in contact with the melt flowing in the die. The die insert is sampled after running out the extrusion experiment, when the melt polymer does not flow any more. The sample is then submitted to scanning electron microscopy coupled with an X-ray microprobe (CAMECA of CAMEBAX type). The detector is a KEVEX energy selective one, Si(Li), with a window for low elements. The accelerating voltage is 25 kV, and the electronic intensity is 0.7 nA.

Polymer Surface Extraction and Analysis

The migration of the leachable components from the surface of PVC to sodium bicarbonate solutions was analyzed after steam sterilization. The sodium bicarbonate concentration was 30 mmol/L and the pH of this solution was 8.25 before the sterilization step. Thirty grams of each extruded sample was immersed in 300 mL of sodium bicarbonate solution. The steam sterilization was achieved in an autoclave of Lequeux type at 115°C, with a sterilization number of 8, for 30 min, with a counter pressure of 3 bars, and the temperature was cooled down to 60°C. After sterilization, the sodium bicarbonate solution was filtered on a Millipore filter, GS WP 04700. The qualitative and quantitative analysis was made through this filter.

Qualitative Analysis

The filter was first analyzed by infrared spectroscopy, using the attenuated total reflection technique (Nicolet 20 SX spectrometer, 400 scans).

Then this filter was analyzed with scanning electron microscopy coupled with an X-ray micro-

probe, as described before. We changed the accelerating voltage and chose 15 kV.

Quantitative Analysis

The filter was put in an oven at 600°C overnight for mineralization, taking care that dusts were not lost. An acidic treatment with hydrochloric acid ultrapure (Aldrich) was done to obtain the corresponding metal ions. This acid medium was then evaporated on an heating plate, and the extract was solubilized in exactly 10 mL of deionized water, giving the solution [noted (S) in the following] that was then submitted to plasma spectroanalyzer of Jobin-Yvon type (JY-24). The oscillating frequency required to generate the plasma from argon is 40.68 MHz, and the power required is 1000 W. Titration of calcium and zinc was done at a wavelength of 393 nm for calcium and 213.8 nm for Zn. The titration was done by the integrated computer system and from the calibration curve. The samples used for calibration were obtained by dilution of standards from Merck for ICP: calcium carbonate 1000 mg/L in solution of nitric acid 5% and zinc 1000 mg/L in nitric acid 5%.

RESULTS AND DISCUSSION

General Comments

In a first experiment set, the barrel temperature was fixed at 140°C and the slit rheometer was equipped with the rough die. At the time t = 0, the PVC formulation with 0.84 phr of stearates was introduced in the feed zone of the extruder. Figure 2(a) and (b) shows the variation of the pressure, recorded by the pressure transducer P2, and the variation of the melt temperature, respectively. From Figure 2(a) it can be observed that the curve of variation of the pressure with time exhibits a maximum at the beginning of the run when the polymer comes through the die. Furthermore, Figure 2(b) shows that the melt temperature increases from 140°C (heating controller temperature) to an average temperature about 158°C. A processing period of about 800 s is required for reaching a steady-state value of both pressure and temperature.

This behavior may be correlated with the fusion torque behavior occurring in an internal mixer such as a Haake plasticorder. Indeed, the torque increases up to a maximum value, which



Figure 2 Flowing inside the rough die: (a) variation of the pressure (P2) vs. processing time; (b) variation of the temperature vs. processing time.

corresponds to the gelation peak, followed by a decrease to a lower plateau value. At the beginning of the extrusion, the set temperature is not reached by the first granules coming at the inlet of the die at 135°C instead of 140°C [Fig. 2(b)], so that the gelation process is delayed. At the steady state of processing, when temperature and pressure are constant, the fusion of PVC takes place inside the extruder, upstream from the die. Chauffoureaux et al.¹⁰ have already reported that a decrease in the extrusion pressure sometimes took place during the first minutes of the runs (about 120 s). Actually, the transient behavior before the steady state depends on the extruder system used.

Furthermore, pressure and temperature curves vs. time exhibits a periodic signal. The periods of

both these signals are rigorously identical and equal to $T_s = 300$ s. The amplitude of both signals is $\Delta p = 4$ bars for pressure and $\Delta T = 3^{\circ}$ C for temperature. The two signals have a phase difference of π . A maximal pressure corresponds to a minimal temperature and vice versa because the apparent viscosity, i.e., the pressure, is obviously temperature dependent. Actually, the oscillation of pressure and temperature signals is caused by the temperature controller and is then inherent to the extruder heating system.

Evidence of Slip Phenomenon

Comparison of the flows in polished and rough dies is very helpful to detect a slip phenomenon, insofar as a rough surface is able to prevent slip. At a fixed apparent shear rate, the occurrence of a slip phenomenon leads to a decrease in the pressure gradient inside the polished die compared to that obtained in the case of the rough die. This decrease in the pressure gradient should be accounted for by a different gelation state of PVC, but this hypothesis is ruled out insofar as gelation takes place upstream from the die at the steady state of extrusion. Comparison of pressure recorded with transducer P2 for the PVC formulation with 0.84 phr of stearates flowing through the rough or smooth die is given in Figure 3. In the polished die, the pressure reached up a steady state in 10^4 s and it is then lower than the pressure measured in the case of the rough die (ΔP = 10 bars). However, no significant difference was observed between temperatures in the two cases.

Furthermore, Figure 4 shows that the pressure gradient at the steady state, measured from the



Figure 3 Variation of the pressure vs. processing time in the rough die and in the polished die (0.84 phr of stearates).



Figure 4 Pressure gradient in the rough die and in the polished die (0.84 phr of stearates). \blacklozenge rough die; \Box polished die.

pressure transducers P2, P3, and P4, is linear. These curves point out that slip occurs inside the polished die at the defined processing conditions of temperature and shear rate, because the pressure gradient inside the polished die is lower than the pressure gradient in the rough die. On the other hand, it was shown in the literature^{6,7} that calcium stearate is able to migrate near the metal surface and, consequently, has an external lubricant role by preventing the polymer melt from sticking to the metal surface. In our case, we may expect calcium and zinc stearates to be responsible for the slip phenomenon, assumption that we will confirm by surface analysis on metal and results on migration in sodium bicarbonate solutions.

To understand slip mechanism promoted by zinc and calcium salts, experiments were performed by varying the stearates concentration. In addition to the previous part, the following stearate concentrations 0.5, 0.3, and 0.15 phr were investigated. For the whole concentrations, the pressure gradient measured in the rough die were found to be independent of stearate concentrations. This result means that the addition of stearate at a lower concentration than 0.84 phr does not modify the viscous behaviour of the PVC compound. Calcium stearate is known to be insoluble in PVC,⁶ and it can be assumed that zinc stearate is not soluble. Indeed, in the case of solid particles in low volume concentration, the bulk viscosity of the compound can be assumed to be independent of the particle concentration.

In the polished die, the flow behavior depends on the stearates concentration, as illustrated for two formulations containing 0.15 and 0.5 phr of



Figure 5 Influence of stearate concentration on slip phenomenon amplitude (polished die).

stearates in Figure 5. The intensity of the pressure peak at the beginning of the extrusion decreases with increasing stearate concentration. Indeed, it has already been shown that calcium stearate can modify the fusion process of PVC.⁶ At the steady state of processing, the pressure decreases with increasing the stearates concentration, meaning that the slip amplitude increases with the stearates concentration. Furthermore, the transient time for reaching the steady state increases with the stearates concentration. Data are reported in Table I. However, the pressure curve for the lowest concentration (0.15 phr) studied here exhibits a singular behavior. Slip of low amplitude ($\Delta p = 3$ bars) is observed during 5 min before the pressure increases with the processing time and finally reaches a constant value. In the steady state, the pressure is close to that measured in the rough die. This result means that a minimal concentration of salts (> 0.15 phr) is required to promote slip of the PVC compound on the metal wall. These first results prove that the zinc and calcium stearate additives are responsible for the slip phenomenon.

Usually in the literature, two types of slip phenomenon are encountered: (1) The additive at the origin of slip migrates and adheres strongly to the metal, leading to a chemically modified surface on which the polymer can slip. In that case, a mini-

Table I Transient Time According to Stearates Concentration ($T_{\text{extrusion}} = 158^{\circ}\text{C}$)

Stearate Concentration	0.15	0.3	0.5	0.84
Transient time (s)	100	400	600	800



Figure 6 Purge experiment. At the arrow symbol the PVC compound (stearate: 0.84 phr) that promotes slip effect is replaced by PVC compound (stearates: 0.15 phr), which does not promote slip effect.

mal concentration of the lubricant additive is required to promote slip, and the slip amplitude is then independent of the lubricant concentration. This coating may be removed after several hours of purging by the same polymer material containing no lubricant agent.

The additive at the origin of slip migrates towards metal and modifies the extreme layer of the polymer (modification of the rheology) in contact with the metal surface. So a lubricant layer of low viscosity can be formed promoting slip. In that case, the lubricant layer on the wall can be easily removed after few minutes of extrusion without additive.^{9,11}

So, it is of importance to estimate the purge time of the slip effect. For example, the PVC compound (stearate concentration phr = 0.84), which



Figure 7 Residence time distribution of the PVC compound inside the extruder, N = 40 rpm, Q = 3 kg/h.



Figure 8 Purge experiment as described in Figure 5 for the formulation containing 0.84 phr of stearates: (a) $T = 165^{\circ}$ C, slip effect; (b) $T = 170^{\circ}$ C, no slip effect.

promotes the maximal slip phenomenon, was extruded during 14000 s. At the steady state, the unlubricated PVC compound (lower concentration of stearates, 0.15 phr) is introduced in the feed zone. The change of compounds was done in the extruder feed zone without interrupting the flow. After changing the lubricated compound by the unlubricated one, the pressure increases with time and reaches after about 10000 s (see Fig. 6) the pressure value expected for a no-slip condition. So, the lubricants that promote slip in the first part of the run were slowly removed from the die wall. Furthermore, from the measure of the residence time distribution (Fig. 7) of the PVC compound in the extruder by a fluorescence method developed elsewhere,⁸ one can evaluate



Figure 9 X-ray dispersive energy spectrum for the formulation containing 0.15 phr of stearates.

the required time to replace a PVC formulation by an other one, as in the previous experiment. The average residence time is about 300 s, and the distribution does not exhibit a tail at the longest times so that one can estimate that the second extruded formulation removes in the extruder the first formulation within 600 s. This time is very short compared with that found previously (10000 s in Fig. 6). Therefore, the formation of a lubricant layer leading to slip is ruled out to describe the phenomenon observed here.

However, as well explained by Rabinovitch et al.,⁶ calcium stearates are salts containing highly polar groups and a long nonpolar hydrocarbon chain. The polar group adheres not only to the polar PVC but also to the polar metal surface displacing PVC melt from the metal surface, preventing it from sticking. These ideas show that slip phenomenon is concentration dependent, and that the lubricant deposited on the metal surface is removed after several hours of purge with a nonlubricated formulation. Rabinovitch finally proposed that the polar groups in calcium stearate are strongly attracted to each other, and form a layered structure such as liquid cristal. From an experimental data

and literature point of view, one can imagine that slip phenomenon is due to stearates coating the metal surface during extrusion.

Temperature Effects

Temperature is one of the most important parameter in polymer processing because temperature can significantly change the rheology of the polymers and the aspects (solid, crystal, liquid) of the different additives. The first set of experiments were performed at the melt temperature T $= 158.0 \pm 1.5$ °C. Now, the melt temperature varies by changing the temperature of the heat controllers. Then the following melt temperatures (temperature at the inlet of the die) were investigated T = 165 and 170°C. In these experiments, slip effect was revealed by purge experiments between lubricated and unlubricated PVC compounds, as defined in the previous part and described in Figure 6. Figure 8(a) and 8(b) show the variation of the pressure with processing time for such experiments at 165 and 170°C, respectively. These curves can be directly compared to the pressure curve at 158°C from Figure 6. Obviously,



Figure 10 X-ray dispersive energy spectrum for the formulation containing 0.84 phr of stearates.

the apparent viscosity, i.e., the pressure in the die, decreases with increasing melt processing temperature. At 165°C; the amplitude of slip is about 5 bars. This amplitude is lower than the amplitude observed at 158°C. Furthermore, the regime of slip is rapidly reached just after the maximal peak at the beginning of the run. The time of purge (about 2000 s) of the slip effect induced by the formulation with 0.84 phr of stearates by the nonlubricated formulation is much lower than the time of purge at 158°C.

At 170°C [Fig. 8(b)], no difference is observed between the pressure for the lubricated or the unlubricated formulation, meaning that the slip effect vanishes with the temperature. At 170°C, slip does not exist at these processing conditions $(\dot{\gamma} = 15 \text{ s}^{-1})$.

By increasing the temperature of the PVC melt, the slip amplitude decreases, meaning that the coating of the wall die produced by stearates is probably noncontinous. This behavior may be accounted for by the evolution of the viscoelasticity of the PVC melt with temperature. Let us imagine that the layer between polymer and metal is caused by an equilibrium steady state between PVC chains moving to the surface and the lubricant particules migrating from the PVC bulk to the surface. By changing the viscoelasticity of the PVC through the temperature effect one can imagine that the equilibrium between polymer chains and lubricant particules is shifted to a higher concentration in PVC chains at the surface. It is well known that the rheology of the PVC changes from an elastic behavior at low temperature to a viscous behavior at high temperature. In a rather elastic behavior, the chains are interdependent by the physical network, whereas in a rather viscous behavior the chains or some chain segments can relax more easily. Furthermore, in the temperature range of 120–180°C, calcium stearates undergoes different structures¹² from cristalline lamellar structure to a ring structure with a mobility of alkoxy groups so that the interactions with PVC can change with the temperature.

Surface Analysis

Die Surface Analysis

A die insert was sampled after the extrusion with the polished die of the two formulations contain-



Figure 11 Infrared spectrum of the filter containing particles issued from the formulation with 0.84 phr of stearates ($T_{\rm extrusion} = 158^{\circ}{\rm C}$) after steam sterilization in sodium bicarbonate.

ing 0.15 phr or 0.84 phr of stearates. The bulk temperature of the formulations was then 158°C, a temperature at which a slip phenomenon was observed in the case of the formulation containing the highest stearates concentration. This die insert was then submitted to scanning electron microscopy coupled with energy dispersive X-ray spectroscopy, as described in the Experimental part. The results are given in Figures 9 and 10, where we can detect the presence of calcium in the two cases. The presence of the Fe, Cr, Si, S, K, and Na is attributed to the insert die response itself. The presence of chlorine shows that the calcium salt is not alone at the die surface, but embedded in PVC polymer chains. The ratio of chlorine over calcium signals seems to be higher in the case of the formulation containing 0.15 phr of stearates, meaning that calcium stearates would be less concentrated at the polymer-metal interface when its concentration in the formulation is smaller. So, from these experiments we can conclude that calcium stearate is responsible for slip phenomenon by migrating onto the die walls. This technique cannot provide the information concerning the lubricant role of zinc stearate.

Analysis of the Stearates Migration in Sodium Bicarbonate Solutions

As described in the Experimental part, we have identified the migration of zinc and calcium stearates through the infrared spectrum of the filter where particles where collected and also through plasma spectroanalysis.

Figure 11 shows the infrared spectrum of the filter issued from the 0.84 phe stearates concentrated formulation. This spectrum is rigorously identical to that of calcium stearate, meaning that the collected particles are mainly calcium stearate. However, it can be seen in Table II that zinc is also detected by plasma spectroanalysis. Calcium and zinc concentrations increase with the stearates concentration in the formulation and also when the extrusion temperature decreases, i.e., when the slip phenomenon amplitude increases, as shown in Table III. The calcium over zinc ratio found in the sodium bicarbonate solution is always higher than that initially introduced in the formulation, suggesting that calcium stearate has a more migrating power than zinc stearate. This observation can be well correlated with the die surface analysis, where only calcium was found. These results also suggest that leachable components of the extruded samples are mainly due to the processing conditions and to their lubricant power towards PVC. These leachables components, including calcium and zinc stearates as suggested by plasma spectroanalysis, have migrated to the surface of the polymer during extrusion and can easily be extracted after a steam sterilization process by a proper aqueous medium.

CONCLUSIONS

By investigating the effect of processing conditions on extrusion characteristics of plasticized PVC compounds, we have developed some correlations between slip effect and migration of PVC

Table IIInfluence of Stearates Concentration on Their Migration in Sodium Bicarbonate Solutionsat Stean Sterilization: Ca and Zn Titration by Plasma Spectroanalysis

Stearates Concentration (phr)	Clean Filter	0.15	0.3	0.5	0.84
Ca (ppm) Zn (ppm)	$\begin{array}{c} 1.1 \ \pm 0.3 \\ 0.04 \ \pm \ 0.005 \end{array}$	$\begin{array}{rrr} 3.5 & \pm \ 0.3 \\ 0.75 & \pm \ 0.2 \end{array}$	$\begin{array}{ccc} 3.0 & \pm \ 0.6 \\ 0.75 & \pm \ 0.2 \end{array}$	$3.9 \pm 0.4 \\ 1.3 \pm 0.4$	$\begin{array}{c} 4.8 \pm 0.4 \\ 1.6 \pm 0.2 \end{array}$

Extrusion Temperature (°C)	Clean Filter	158	165	170
Ca (ppm) Zn (ppm)	$\begin{array}{c} 1.1 \ \pm 0.3 \\ 0.04 \pm 0.005 \end{array}$	$\begin{array}{c} 4.8 \pm 0.4 \\ 1.6 \pm 0.2 \end{array}$	$5.3 \pm 0.7 \\ 1.4 \pm 0.2$	$\begin{array}{c} 4.5 \pm 0.5 \\ 0.9 \pm 0.3 \end{array}$

Table IIIInfluence of Extrusion Temperature of the Formulation Based on 0.84 phr of Stearates onTheir Migration in Sodium Bicarbonate Solutions

additives such as zinc and calcium stearates. Rough and polished dies were used to reveal slip effect, and it was proved that zinc and calcium stearate can promote the slip effect of the PVC on the polished die wall. Slip occurs above a critical concentration (0.15), and its amplitude increases with increasing stearate concentration. It was also observed that slip amplitude decreases and vanishes with increasing melt temperatures. From these experiments we can suppose that slip effect is induced by the stearates coating the metal surface of the die.

Surface analysis of the die metal has qualitatively confirmed the presence of calcium stearate only. On the other hand, extraction of calcium and zinc stearates by aqueous solutions with alkaline pH, such as sodium bicarbonate, was achieved during a sterilization step by autoclave. They were identified by infrared spectroscopy and quantified by titration of calcium and zinc elements through plasma spectroanalysis. These measurements are well correlated to the variation of the total amount of stearates in the formulation and to the extrusion temperature, which means to the slip phenomenon amplitude.

So, if calcium and zinc stearates have the low toxicity required for the development of infusion fluid bags, this work shows that their use can be limited in this area due to their lubricant ability and extraction by aqueous media such as sodium bicarbonate solutions.

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