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Initial evaluation of USP apparatus 4 for measuring dissolution profile of man-made vitreous fibers

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ABSTRACT

We report the successful evaluation of a US Pharmacopeia Apparatus 4 (USP-4) system in measuring the dissolution profiles of man-made vitreous fibers (MMVF)[1]. Glass and stone wool fibers with different (high- and low-) solubility profiles were tested in closed-loop configuration using a sodium/potassium phosphate buffer solution or an acetate buffer, respectively. Results confirm a need to operate in diluted conditions to avoid silicon saturation in the simulant solution and suppression of fiber dissolution. A clear fiber-to-fiber differentiation with good cell-to-cell reproducibility was achieved. These findings support the continued development of a USP-4 protocol for MMVF in vitro acellular testing.

1. Introduction

A robust in vitro measurement of the dissolution rate constants of man-made vitreous fibers (MMVF) offers a means of adhering to the 3R's of in vivo tests vis a vis determining biopersistence without using animals. Today, compliance to (*Note Q*, EC no. 1272/2008) regulatory requirements may only be demonstrated via in vivo biopersistence testing. Measured in vitro dissolution rate constants (K_{dis}) correlate to fiber biopersistence, which is a key factor in understanding the pathogenicity of MMVF (Donaldson and Tran, 2004; Maxim et al., 2006; Bernstein et al., 1996; Davis, 1994; Eastes et al., 1995). Current in vitro acellular methods have shown predictive power versus in vivo biopersistence test results (Hesterberg and Hart, 2000; Madl and O'Neill, 2023). However, these methodologies (Sebastian et al., 2002; Potter, 2000; Scholze, 1988; Scholze and Conradt, 1987) have not yet been sufficient to be accepted by regulators as viable replacement for required in vivo tests (Andersen et al., 2002). Key challenges with the current methods include limited interlaboratory and intralaboratory reproducibility (Guldberg et al., 2003).

In researching means of improving test reproducibility, we have identified dissolution testing using the USP Apparatus 4 (USP-4) as a possible means of producing a highly repeatable in vitro acellular dissolution test. The USP Apparatus 4 is a robust and regulatory accepted system for dissolution testing in pharmaceutical applications (Kramer et al., 2005; Miller et al., 2020; Aldeek et al., 2021). It can be used, with an appropriate method, to evaluate the dissolution profiles of

Abbreviations: USP-4, US pharmacopeia apparatus 4; MMVF, Man-made vitreous fibers; SA/V, fiber surface area to solution volume ratio; K_{dis}, dissolution rate constant; ICP-OES, Inductively coupled plasma optical emission spectroscopy.

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[1] Man-made vitreous fibers (MMVF) is the terminology commonly used in the European Union to refer to mineral wool fibers, it is also the terminology used in the classification entries for these materials in Regulation (EC) No 1272/2008 classification, labelling and packaging of substances and mixtures as the term synthetic vitreous fibers (SVF) is also used in literature and other jurisdictions to refer to mineral wool fibers.

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Table 1
Chemical composition, specific surface area and solubility for the tested fibers, following Guldberg et al., 2003 (Guldberg et al., 2003).

Type	Sample name	Solubility (Guldberg et al., 2003)	Chemical composition (Guldberg et al., 2003), major oxides wt %								Specific surface area (Guldberg et al., 2003), cm^2/g
			SiO_2	Al_2O_3	CaO	MgO	FeO*	Na_2O	K_2O	B_2O_3	
Glass wool	K-2 345	Poor	63.6	3.3	7.7	3.1	0.2	15.8	1.5	4.6	2780
	994007	High	62.2	0.9	7.5	3.0	<0.1	15.5	0.4	9.4	3010
Stone wool	FI980889	Poor	45.8	14.9	14.3	10.9	7.6	2.0	1.0	-	2270
	MMVF34 * *	High	39.9	22.8	14.6	8.7	7.6	2.5	0.9	-	2710 * *

* Fe is present as Fe(II) in stone wool samples.
** MMVF34 fibers were produced in 2017 by ROCKWOOL A/S and have the similar composition but different specific surface area as the soluble fibers reported in Guldberg et al., 2002 (Guldberg et al., 2002).

many dosage forms, including longer-acting inhaled forms. We see a clear parallel to existing flow-through test methods for MMVF when comparing the design of Apparatus 4. In this parallel we see potential to develop test protocols based on Apparatus 4 to robustly assess the dissolution rate profiles of MMVF. Apparatus 4 is built in a standardized manner in order to generate consistent data to support the regulatory approval process of pharmaceutical products. For this reason, it is a good candidate to generate repeatable and reproducible results on fiber dissolution.

It is well understood that robust design of in vitro acellular dissolution tests for MMVF requires consideration and control of several key variables. These include temperature, fiber surface area to solution volume ratio (SA/V), pH, flow rate, and simulant fluid design (pH, complexing agents, buffers, etc.) (Okhrimenko et al., 2022a, 2022b; Guldberg et al., 1998; Steenberg et al., 2001; Barly et al., 2019; Koch et al., 2021; Potter and Mattson, 1991; Mattson, 1994; De Meringo et al., 1994). The scope of this screening study was limited to proving that MMVF can be used in the USP Apparatus 4 system with conventional measurement practice, and then to understand if fiber-fiber differentiation is achievable. Detailed exploration of other key variables is beyond the current scope, but recognized as critical to final protocol development. Positive results versus the goals of measuring MMVF successfully, with clear fiber-fiber differentiation, will demonstrate feasibility, and further motivate work to develop a robust protocol based on Apparatus 4.

2. Material and methods

Glass and stone wool fibers used in previously-published in vitro studies were selected for this work (Guldberg et al., 2003, 2002). Fiber identification and properties are summarized in Table 1. Fibers with low and high solubility at neutral and acidic pH, based on earlier results, were selected to facilitate demonstrating fiber-fiber differentiation. All fibers were produced without binder and other organic treatment. Stone wool samples were sieved prior to analysis to remove shot and coarse non-fibrous material. Glass wool samples were crushed mechanically prior to the analysis, to reduce fiber lengths. Fiber dosing was based on fiber mass, and not on a fixed surface area to fluid volume ratio as is typical for glass dissolution studies (Okhrimenko et al., 2022b; Guldberg et al., 1998; Steenberg et al., 2001; Barly et al., 2019). However, the small difference in specific surface area per Table 1 suggests only a minimal difference in SA/V when comparing glass wool samples or stone wool samples.

Traditionally, in vitro acellular dissolution tests on fibers use complex solutions such as Gamble's (Boisa et al., 2014) or Kanapilly's (Kanapilly et al., 1973) solutions derived from invasive biological studies. For this work, we instead chose simplified buffers as typically employed with Apparatus 4 for batch release testing. While not typical of simulant fluids used for particle or fiber dissolution studies directed toward respiratory systems, they offer simple, robust buffers proven to work well for dissolution studies in the pharmaceutical context (Mendonça et al., 2011; Stippler et al., 2004; Medina-López et al., 2020).

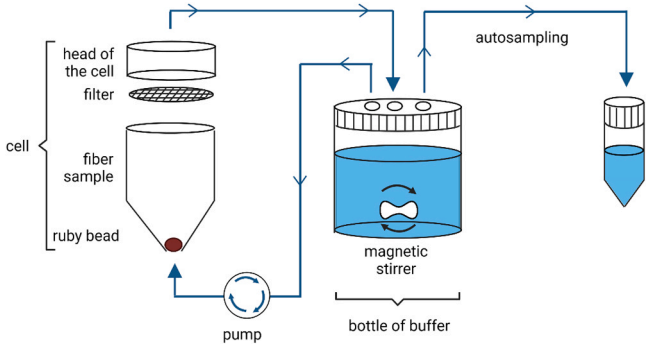

Fig. 1. General schematic of USP-4 in a closed loop setup during MMVF dissolution testing.

Dissolution tests on the glass wool samples were performed using either a potassium phosphate or sodium phosphate buffer at near-neutral pH (7.4). Stone wool dissolution testing employed acetate buffer pH 4.5. Details on buffer formulation are included in Table S1. The pH values were chosen in accordance with the in vivo dissolution of fibers in two different milieus present in the lungs: pH 7.4 is typical for extra-cellular environment (Nguea et al., 2008) and pH 4.5 is found in the microenvironment of the intracellular phagolysosome compartments of macrophages (Etherington et al., 1981; Oberdörster, 1991).

Measurement methodology was generally based on the USP <1092> chapter "The dissolution procedure: Development and Validation". General goals were to establish parameters leading to reproducible dissolution profiles with clear fiber-fiber differentiation. The compendial flow through cell method described in European Pharmacopeia (chapter 2.9.3) as well as in the US Pharmacopeia (chapter <711>) was used. This method will be referred to through this report as either "flow-through cell" or as "USP-4 method".

As a first screening, dissolution tests were carried out for either 7 or 14 days at 37 ± 0.5 °C using a SOTAX CE7 Smart USP-4 apparatus at closed loop configuration which was equipped with 7 standard 22.6 mm diameter cells and piston pumps (SOTAX CP7–35) with automated sample collection (Fig. 1). Fibers are deposited in the cells and maintained in this space by a single ruby bead at the cone apex and a filter at the head of the cell. To optimize dissolution test parameters for glass wool, different mass of fibers (25–100 mg), flow rate (4–8 ml/min), buffer volume (250–500 ml) and type of filters (0.2–1.2 μm) were used (Table S2). For the stone wool testing, optimal parameters determined earlier for glass wool samples were adopted without further modification (Table S3). No glass components (transparent beads, bottles for the fluids, storage equipment, etc.) were used in the set-up of the apparatus to avoid potential cross-contamination.

Periodic sampling of the solution (at day 1, 4, 7, 11 and 14 for glass wool; at 4 h and day 1, 4, 5, 6, 7 for stone wool) was conducted to monitor pH and the level of glass constituents dissolved in solution, in particular Si as a major component of glass and stone wool that de-

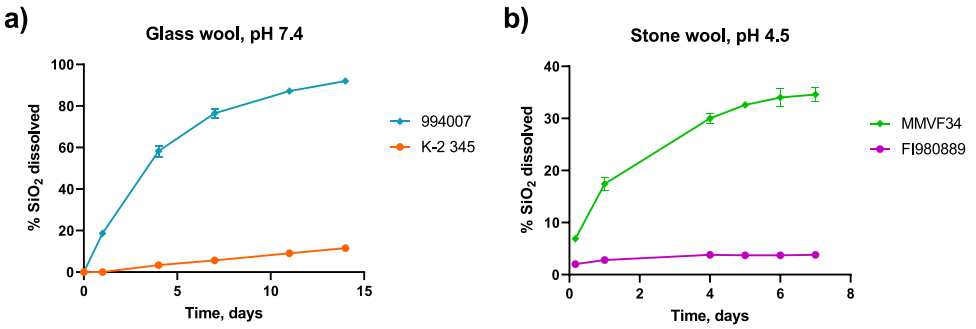

Fig. 2. Mean dissolution profiles of a) glass wool, K-2 345 and 994007, in Na-Phosphate buffer pH 7.4 (Run 6) and b) stone wool, MMVF34 and FI980889, in acetate buffer pH 4.5. The results are obtained with USP-4 apparatus at 37 °C using 22.6 mm diameter cells, 25 mg fiber load, 500 ml of the buffer, 8 ml/min flow rate and 1.2 μm cellulose filters in 3 parallel runs. The error bars for FI980889 and for K-2 345 are smaller than the symbols.

termines fiber integrity. Because analyses of glass and stone wool leachates were done in different laboratories, different procedures were utilized. For glass wool leachates analysis, small aliquots (1.2 ml) were diluted into 10 ml of 2 % nitric acid, and then measured via ICP-OES. For stone wool leachates analysis, aliquots were larger (10 ml) and were analyzed with ICP-OES without acidification and dilution. The extent of the dissolution was calculated using Si concentration and expressed as percentage of dissolved SiO_2 from the fibers:

$$\%diss.SiO_2 = \frac{C_{Si} \bullet M_{SiO_2} \bullet V \bullet 100}{m_0 \bullet (wt.\%_{SiO_2}/100)} \quad (1)$$

where C_{Si} stands for Si concentration in the solution (mol/l); M_{SiO2}, molar mass of SiO_2 (60 g/mol); V, solution volume (l) at probing taking into account the probes volume taken at previous steps; m_0, fiber mass load (g); $wt\ \%\ SiO_2$, weight percent of SiO_2 in fiber bulk composition (Table 1).

3. Results and discussion

During the initial series of glass wool dissolution tests, some challenges were encountered. Results from Run 1 (per Table S2), done using a relatively large sample mass and a small amount of the buffer (100 mg and 250 ml), showed a quick saturation (130 ppm Si) of the buffer solution in the respect to amorphous SiO_2 (115 ppm at 25 °C (Morey et al., 1964); 187 ppm at 50 °C (Sjöberg, 1996)). This in turn led to a plateau of Si concentration and cessation of dissolution (Fig. S1). To avoid SiO_2 saturation stopping dissolution, fiber load was progressively reduced to 50 mg (Run 2 in Table S2) and further to 25 mg (Runs 3 – 6 in Table S2), while solution volume was increased to 500 ml. This increase in dilution resulted in elimination of the Si concentration plateau. The absence of the plateau is necessary to distinguish between high and poor soluble glass wool samples (Fig. S2).

Some issues with back pressure were also encountered. Runs 3–6 were aimed at resolving occasional clogging issues (Fig. S3), generally through filter modification and flow rate change. It was unclear on reflection if these sporadic clogging issues are rooted in the measurement of fiber, or were simply special-case issues.

The resolution of these challenges led us to use parameters from the later runs to examine fiber-fiber differentiation. Test conditions for examining glass wool differentiation included: 25 mg of glass wool sample, 500 ml of buffer solution (Na-phosphate, pH 7.4) with flow rate 8 ml/min and filtration through 1.2 μm cellulose acetate filter (Run 6 in Table S2).

The dissolution profiles of 994007 and K-2 345 glass wool samples in Na-Phosphate buffer pH 7.4 under these conditions are presented in Fig. 2a. The pH of the buffer was within the 7.4 ± 0.5 pH range (Fig. S4). As expected, clear fiber-to-fiber differentiation was observed (Fig. 2).

Test conditions determined for the stone wool samples were derived from the glass wool work, save the change to the acetate buffer at pH 4.5 (Table S3). Stable pH 4.50 ± 0.05 was observed throughout the duration of the tests (Fig. S5). The dissolution profiles of MMVF34 and FI980899 fiber are shown in Fig. 2b. Again, per Fig. 2, clear fiber-fiber differentiation was achieved for stone wool fibers.

As expected, these results obtained using the USP-4 apparatus are in agreement with solubility data from the literature (Guldberg et al., 2003). At Day 7, 80 % of highly soluble 994007 and 9 % of poorly soluble K2–345 glass wool fibers were dissolved. For the stone wool fibers, the dissolved amount after Day 7 is 40 % for highly soluble MMVF34 and only 4 % of poorly soluble FI980889. For all samples, glass and stone wools, little cell-to-cell variation was noted (Figs. S2-3 for glass wool and Fig. S6 for stone wool) compared to the clear fiber-to-fiber differentiation.

4. Conclusions

Overall, the results from this study were positive vis a vis demonstrating the potential for using USP Apparatus 4 system for assessing the dissolution profile of MMVF. The two encountered challenges were successfully mitigated. Changes to reduce sample size, modify flow rate, and increase filter pore size were sufficient to mitigate the clogging observed during the initial runs. While all changes were expected directionally to reduce pressure in the circulating system, the experimental design was not sufficient to identify the variable(s) most directly leading to this improvement. The data does however provide guidance as a known-good condition for the next phase of development. Reduction in the sample-to-solution ratio by both increasing simulant fluid volume and reducing sample mass were observed to impact the resulting dissolution profile (Fig. S1 and S3). This supports the hypothesis that when reaching silica saturation, dissolution was suppressed, as all subsequent runs were completed well below that threshold, and with generally repeatable dissolution profiles. This now forms an important process criterion for additional development.

The selected fibers, which from previous works were known to be clearly differentiated, were clearly distinguished in this work. The greater than 5 times difference in the percentage of silica dissolved at 7 days exceeds the within run cell-to-cell variation. In conclusion, these results support a strong work program to further develop the potential of the Apparatus 4 system for the measurement of the dissolution of MMVF. Future investigations using the Apparatus 4 will be focused on studying effects of simulant fluid composition, pH and fiber sample surface area-to-solution volume ratio on MMVF dissolution.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: JH is employed by Owens Corning, DVO and MS are employed by ROCKWOOL A/S, EC and QH are employed by Saint-Gobain, ND is employed by Knauf Insulation, EP participated to the project via remunerated with Knauf Insulation, AA and NM are employed by URSA Insulation S.A., manufacturers of man-made vitreous fibers. SH and ML are employed by SOTAX Pharma Services a service provider that performs dissolution and release testing from pharmaceutical dosage forms with USP-4. JdC, LH and AAB have been participating in this project through remunerated employment and/or contractual relationships with Eurima, the European Insulation Manufacturers Association.

Data Availability

Data will be made available on request.

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Appendix A. Supplementary data

Buffers' chemical composition, USP-4 parameters adjustment tables, pH and dissolution profiles of glass wool during optimization are presented in Supplementary data.

Appendix B. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.toxlet.2023.09.005.

References

Aldeek, F., McCutcheon, N., Smith, C., Miller, J.H., Danielson, T.L., 2021. Dissolution testing of nicotine release from OTDN pouches: product characterization and product-to-product comparison. Separations 8 (1), 7.

Andersen, A., Axten, C., Bernstein, D.M., Brochard, P., Castranova, V., Donaldson, K., Dumortier, P., Everitt, J.I., Gustavsson, P., Hesterberg, T.W., Jaurand, M.C., Kane, A. B., Marsh, G.M., Morimoto, Y., Muhle, H., Oberdörster, G., Olin, S., Savolainen, K. M., Schneider, T., 2002. IARC monographs on the evaluation of carcinogenic risks to humans. In: World Health Organization International Agency for Research on Cancer, vol. 81. IARCPress, Lyon, France (Man-made Vitreous Fibers).

Barly, S.H., Okhrimenko, D.V., Solvang, M., Yue, Y., Stipp, S.L., 2019. Dissolution of stone wool fibers with phenol-urea-formaldehyde binder in a synthetic lung fluid. Chem. Res. Toxicol. 32 (12), 2398–2410.

Bernstein, D.M., Morscheidt, C., Grimm, H.-G., Thévenaz, P., Teichert, U., 1996. Evaluation of soluble fibers using the inhalation biopersistence model, a nine-fiber comparison. Inhal. Toxicol. 8 (4), 345–385.

Boisa, N., Elom, N., Dean, J.R., Deary, M.E., Bird, G., Entwistle, J.A., 2014. Development and application of an inhalation bioaccessibility method (IBM) for lead in the PM10 size fraction of soil. Environ. Int. 70, 132–142.

Davis, J., 1994. The role of clearance and dissolution in determining the durability or biopersistence of mineral fibers. Environ. Health Perspect. 102 (suppl 5), 113–117.

De Meringo, A., Morscheidt, C., Thélohan, S., Tiesler, H., 1994. In vitro assessment of biodurability: acellular systems. Environ. Health Perspect. 102 (Suppl 5), 47.

Donaldson, K., Tran, C.L., 2004. An introduction to the short-term toxicology of respirable industrial fibres. Mutat. Res./Fundam. Mol. Mech. Mutagen. 553 (1), 5–9.

Eastes, W., Morris, K.J., Morgan, A., Launder, K.A., Collier, C.G., Davis, J.A., Mattson, S. M., Hadley, J.G., 1995. Dissolution of glass fibers in the rat lung following intratracheal instillation. Inhal. Toxicol. 7 (2), 197–213.

Etherington, D., Pugh, D., Silver, I., 1981. Collagen degradation in an experimental inflammatory lesion: studies on the role of the macrophage. Acta Biol. Et. Med. Ger. 40 (10–11), 1625–1636.

Guldberg, M., Christensen, V.R., Perander, M., Zoitos, B., Koenig, A.R., Sebastian, K., 1998. Measurement of in-vitro fibre dissolution rate at acidic pH. Ann. Occup. Hyg. 42 (4), 233–243.

Guldberg, M., Jensen, S.L., Knudsen, T., Steenberg, T., Kamstrup, O., 2002. High-alumina low-silica HT stone wool fibers: a chemical compositional range with high biosolubility. Regul. Toxicol. Pharmacol. 35 (2), 217–226.

Guldberg, M., Madsen, A.L., Sebastian, K., Fellman, J., Potter, R., Corning, O., Bauer, J., Manville, J., Searl, A., Maquin, B., 2003. In-vitro dissolution of vitreous silicate fibres according to EURIMA test guideline: results of two round robins. Glass Sci. Technol. 76 (4), 199–205.

Hesterberg, T., Hart, G., 2000. Lung biopersistence and in vitro dissolution rate predict the pathogenic potential of synthetic vitreous fibers. Inhal. Toxicol. 12 (sup3), 91–97.

Kanapilly, G., Raabe, O., Goh, C., Chimenti, R., 1973. Measurement of in vitro dissolution of aerosol particles for comparison to in vivo dissolution in the lower respiratory tract after inhalation. Health Phys. 24 (5), 497–507.

Koch, C., Okhrimenko, D.V., Solvang, M., Aznar, A., Pezennec, E., Chaudan, E., Magrane Francesch, J., Lindberg, P., Herault, Q., Alami Badissi, A., 2021. Comment on critical choices in predicting stone wool biodurability: lysosomal fluid compositions and binder effects. Chem. Res. Toxicol.

Kramer, J., Grady, L., Gajendran, J., 2005. Historical development of dissolution testing dalam pharmaceutical dissolution testing editor dressman, J dan Kramer. J. Taylor & Francis Group, LLC.

Madl, A.K., O'Neill, H.C., 2023. Fiber biodurability and biopersistence: historical toxicological perspective of synthetic vitreous fibers (SVFs), the long fiber paradigm, and implications for advanced materials. Crit. Rev. Toxicol. 1–56.

Mattson, S.M., 1994. Glass fiber dissolution in simulated lung fluid and measures needed to improve consistency and correspondence to in vivo dissolution. Environ. Health Perspect. 102 (suppl 5), 87–90.

Maxim, L.D., Hadley, J.G., Potter, R.M., Niebo, R., 2006. The role of fiber durability/biopersistence of silica-based synthetic vitreous fibers and their influence on toxicology. Regul. Toxicol. Pharmacol. 46 (1), 42–62.

Medina-López, R., Guillén-Moedano, S., Hurtado, M., 2020. In vitro release studies of furosemide reference tablets: influence of agitation rate, USP apparatus, and dissolution media. Admet dmpk 8 (4), 411–423.

Mendonça, T.F., Barros, E.G. d, Pereira, G.R., Araújo, M.B. d, Bonfilio, R., 2011. Development and validation of a dissolution test for diltiazem hydrochloride in immediate release capsules. Quím. Nova 34.

Miller, J.H., Danielson, T., Pithawalla, Y.B., Brown, A.P., Wilkinson, C., Wagner, K., Aldeek, F., 2020. Method development and validation of dissolution testing for nicotine release from smokeless tobacco products using flow-through cell apparatus and UPLC-PDA. J. Chromatogr. B 1141, 122012.

Morey, G., Fournier, R., Rowe, J., 1964. The solubility of amorphous silica at 25C. J. Geophys. Res. 69 (10), 1995–2002.

Nguea, H., de Reydellet, A., Le Faou, A., Zaiou, M., Rihn, B., 2008. Macrophage culture as a suitable paradigm for evaluation of synthetic vitreous fibers. Crit. Rev. Toxicol. 38 (8), 675–695.

Oberdörster, G., 1991. Deposition, elimination and effects of fibres in the respiratory tract of humans and animals. VDI-Ber. 853, 13–37.

Okhrimenko, D.V., Barly, S.H.Q., Jensen, M., Lakshtanov, L.Z., Johansson, D.B., Solvang, M., Yue, Y.Z., Stipp, S.L.S., 2022a. Surface evolution of aluminosilicate glass fibers during dissolution: Influence of pH, solid-to-solution ratio and organic treatment. J. Colloid Interface Sci. 606, 1983–1997.

Okhrimenko, D.V., Bøtner, J.A., Riis, H.K., Ceccato, M., Foss, M., Solvang, M., 2022b. The dissolution of stone wool fibers with sugar-based binder and oil in different synthetic lung fluids. Toxicol. Vitr. 78, 105270.

Potter, R.M., 2000. Method for determination of in-vitro fiber dissolution rate by direct optical measurement of diameter decrease. Glass Sci. Technol. (Frankf.) 73 (2), 46–55.

Potter, R.M., Mattson, S.M., 1991. Glass fiber dissolution in a physiological saline solution. Glastech. Ber. 64 (1), 16–28.

Scholze, H., 1988. Durability investigations on siliceous man-made mineral fibers: a critical review. Glastech. Ber. 61 (6), 161–171.

Scholze, H., Conradt, R., 1987. An in vitro study of the chemical durability of siliceous fibres. Ann. Occup. Hyg. 31 (4B), 683–692.

Sebastian, K., Fellman, J., Potter, R., Bauer, J., Searl, A., Meringo, A. d, Maquin, B., Reydellet, A. d, Jubb, G., Moore, M., 2002. EURIMA test guideline: in-vitro acellular dissolution of man-made vitreous silicate fibres. Glastech. Ber.

Sjöberg, S., 1996. Silica in aqueous environments. J. Non-Cryst. Solids 196, 51–57.

Steenberg, T., Hjenner, H.K., Jensen, S.L., Guldberg, M., Knudsen, T., 2001. Dissolution behaviour of biosoluble HT stone wool fibres. Glass Sci. Technol. 74 (4), 97–105.

Stippler, E., Kopp, S., Dressman, J., 2004. Comparison of US pharmacopeia simulated intestinal fluid TS (without pancreatin) and phosphate standard buffer pH 6.8, TS of the international pharmacopoeia with respect to their use in in vitro dissolution testing. Dissolution Technol. 11, 6–10.