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ORIGINAL ARTICLE

Cellulose acetate-based composites with antimicrobial properties from embedded molybdenum trioxide particles

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Significance and Impact of the Study: In this study, development of a novel thermoplastic bio-based composite with excellent antimicrobial surface properties is investigated. To the best of our knowledge, this is the first report to evaluate the antimicrobial properties of molybdenum trioxide embedded into a cellulose acetate as biopolymer matrix. The developed composites might step up to innovative applications used in modern medical and public environments.

Keywords
antimicrobial materials, biopolymer composite, cellulose acetate, local acidity, molybdenum trioxide, nanostructures, specific surface area.

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Abstract

The objective of this research was to develop novel cellulose acetate (biopolymer) composite materials with an excellent antimicrobial activity by embedding molybdenum trioxide particles with unique high specific surface area. High surface area molybdenum trioxide particles were prepared from freshly precipitated molybdenum trioxide dihydrate ($MoO_3 \cdot 2H_2O$) and subsequent calcination at 340°C under H_2/N_2 gas. Microbiological evaluation against *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* were performed applying a roll-on test and excellent antimicrobial activities were determined for composites with embedded anhydrous molybdenum trioxide with a high specific surface area. Cellulose acetate composites comprising MoO_3 particles can eliminate three harmful bacteria as a result of the release of protons from the material and surface enlargement of the molybdenum trioxide particles. The findings support a proposed antimicrobial mechanism based on local acidity increase due to large specific surface areas.

Introduction

The number of health care-associated (nosocomial) infections and their prevention approaches have been rapidly increasing in recent years due to the huge impact on the prosperity of patients and environmental safety issues (Klevens *et al.* 2007). Recent reports from the United States indicate that nosocomial infections account for two million per year, of which almost half were acquired through bacterial transmission from medical devices and other health care-related products (Gorman and Jones 2002; Magill *et al.* 2014). On the one hand, it is conferred that the use of antibiotics must be drastically reduced due to the formation of multiple resistant pathogens. On the other hand transmission of pathogen from devices and products used in medical environments should be diminished. The growth of pathogen-containing biofilms has gained much attention among scientists and medical personnel to develop novel material composites presenting antibacterial properties on their surface. The antimicrobial properties of metal and metal oxides particles, such as Ag, Cu, Au, TiO_2, ZnO, MgO and CuO, embedded in polymer matrices have been investigated extensively in the past decade (Bechert *et al.* 2000; Kalaycı *et al.* 2010; Delgado *et al.* 2011; Raghupathi *et al.* 2011; Hazer *et al.* 2012; Das *et al.* 2013; Lackner and Guggenbichler 2013a; Shafaei *et al.* 2014a). However, these materials have several intrinsic drawbacks, such as low active surface area, low adherence on the substrate surfaces, high cytotoxicity and high production cost. It was recently reported that molybdenum oxides exhibit significant antibacterial activities (Guggenbichler *et al.* 2010; Lackner and Guggenbichler 2013b,c; Lackner *et al.* 2013). In our previous studies we confirmed that molybdenum trioxide particles embedded

in thermoplastic polyurethane or deposited on titanium surfaces exhibit highly promising antimicrobial properties towards *S. aureus*, *E. coli* and *Ps. aeruginosa*. Furthermore, we found that the potentials of the molybdenum oxides to reduce the number of live bacteria are directly affected by the annealing temperature and time in different crystalline structures (Lorenz *et al.* 2011; Zollfrank *et al.* 2012; Gutbrod and Zollfrank 2013; Shafaei *et al.* 2013b, 2016c). Recently, the antimicrobial activity of a molybdenum trioxide coating on lead wires investigated against 11 different micro-organisms responsible for nosocomial infections. It was found that the biocidal effect was fastest (2 h after contact with the micro-organism) against the Gram-positive *Staph. aureus* and *E. faecium*, while it took longer (6 h after contact with the micro-organism) against Gram-negative micro-organisms (Tétault *et al.* 2012). Similarly, the antibacterial properties of MoO_3 and MoO_3 nanoplates (paint) reported against different types of bacteria and evaluated the minimum inhibitory concentration between 8 and 16 μg ml^{-1} of MoO_3 and the mechanism of MoO_3 toxicity by measuring the β-D-galactosidase activity (Krishnamoorthy *et al.* 2013a, 2014b). Very recently, antimicrobial activities of molybdenum-tungsten oxides and suboxides investigated with different morphologies and crystalline structures against *E. coli*, suggested that the local acidity can be related to their antimicrobial properties due to the enrichment in large grains of molybdenum oxides with different stoichiometry and release of free radicals from the $W_{18}O_{49}$ phase under visible light (Mardare and Hassel 2014). Molybdenum and most molybdenum compounds in general show a low cytotoxicity and exhibit a high general biocompatibility with human organisms, animals and plants with antibacterial activity for biomedical applications (Gupta and Gupta 1998; Barceloux 1999; Kapp 2005; Heijerick *et al.* 2012; Ribeiro *et al.* 2016). Moreover, molybdenum trioxide and their compounds such as poly (ethylene glycol) (PEG)-functionalized MoO_{3-x} hollow nanospheres (PEG-MoO_{3-x} HNSs) can be used either as on-demand theranostic nanoagents with imaging, drug carrier and photothermal therapy (PTT) functions in the treatment of lung and breast cancer iMCF-7 cells (Tran *et al.* 2014; Bao *et al.* 2016; Fakhri and Nejad 2016). Mo is also an essential cofactor for several enzymes such as xanthine oxidase, sulphite oxidase, aldehyde oxidase, pyranopterin and molybdenum-containing nitrogenases in mammals (Wuebbens *et al.* 2000; Hänzelmann and Schindelin 2004; Boll *et al.* 2005; Kirk and Stein 2013). Furthermore, complexes of molybdenum (VI) have been used as an effective antidiabetic agent (Levina *et al.* 2007).

The preparation of novel biopolymer materials from renewable feedstock has attracted great attention in recent years due to their promising application prospects and environmental benefits. Biopolymers are used in food packaging materials, biological, pharmaceutical and medical applications ranging from simple sutures assisting in wound healing to complex artificial heart valves in surgery or orthopaedic devices. The extensive use of biopolymers has resulted in significant improvements in longevity and quality of living for patients (Repetto *et al.* 2001; Gorman and Jones 2002; Treacy and Goldberg 2006; Rodríguez *et al.* 2014). Plant-derived biopolymers such as cellulose derivatives exhibit proficient properties such as thermoplasticity, low toxicity, biodegradability, biocompatibility and mucoadhesivity (Vieira *et al.* 2011). Therefore, composite biopolymers with embedded antibacterial agents could be promising and attractive candidates for the replacement of cytotoxic, inactive and expensive materials. However, the microbial infection of biopolymers is still one of the most serious complications for the use in biomaterials in modern medicine. Effective strategies to reduce the number of nosocomial infections are necessary. One approach to reduce bacterial colonization is to modify the surface chemistry and roughness of biomaterial substrates. Extensive studies are available, which suggest that highly active metal and metal oxide particles on the polymer surfaces exhibit excellent antimicrobial properties (Bechert *et al.* 2000; Kalaycı *et al.* 2010; Hazer *et al.* 2012). The objective of this study was to develop a novel thermoplastic bio-based composite with antimicrobial surface properties. These will also be nontoxic, biocompatible and be prepared from transition metal oxides such as molybdenum trioxide, which have been recently reported to exhibit excellent antimicrobial properties.

Results and Discussion

SEM micrographs of the MoO_3 dihydrate and the anhydrous MoO_3 (Fig. 1a, b) reveal the distinct plate-like shapes of the particles. During a thermal decomposition of the dihydrate to the anhydrous MoO_3, delamination and a series of parallel cracks are formed and the sizes of the particles are changed. At the same time, the specific surface area of the particles is drastically increased from 2·5 to 180·2 m^2 g^{-1}.

Backscattered electron–scanning electron microscope (BSE–SEM) micrographs of sample Cellulose acetate – Triacetine – Molybdenum trioxide (CA-TA-MoO_3) show even dispersion of molybdenum trioxide particles on the surface of the composite before and after storage of specimens under water for 2 months, Figs 2a, b. Analysis of the storage liquids samples confirmed a concentration of 0·6202 mg l^{-1} molybdenum for those samples as determined by AAS and inductively coupled plasma optical emission spectrometry (ICP-OES) measurements.

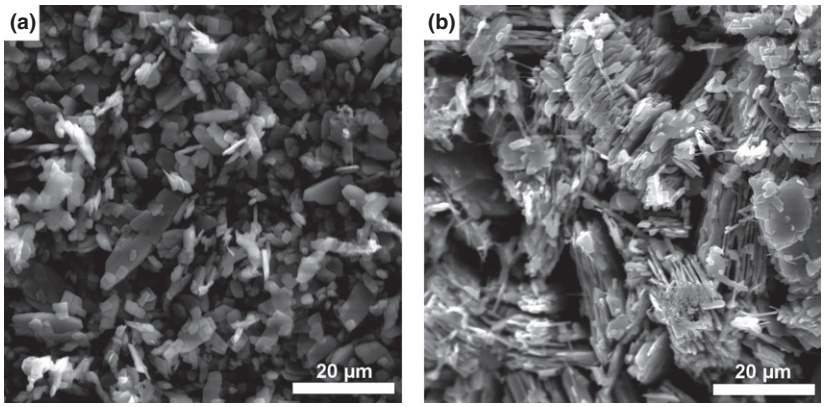

Figure 1 SEM micrographs of as-synthesized $MoO_3 \cdot 2H_2O$ (a) and calcined MoO_3 (b) shows that the cracks correspond to specific surface area and ultimately its high antimicrobial activity.

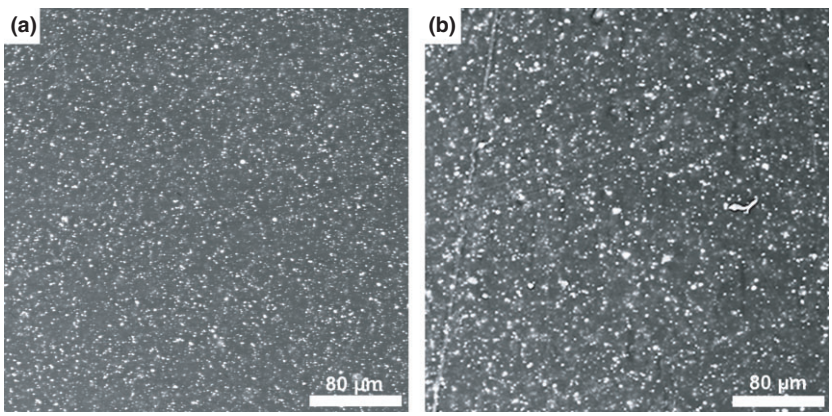

Figure 2 BSE-SEM micrographs of the surfaces of the CA matrix with embedded MoO_3 particle before (a) and after (b) storage under water for 2 months.

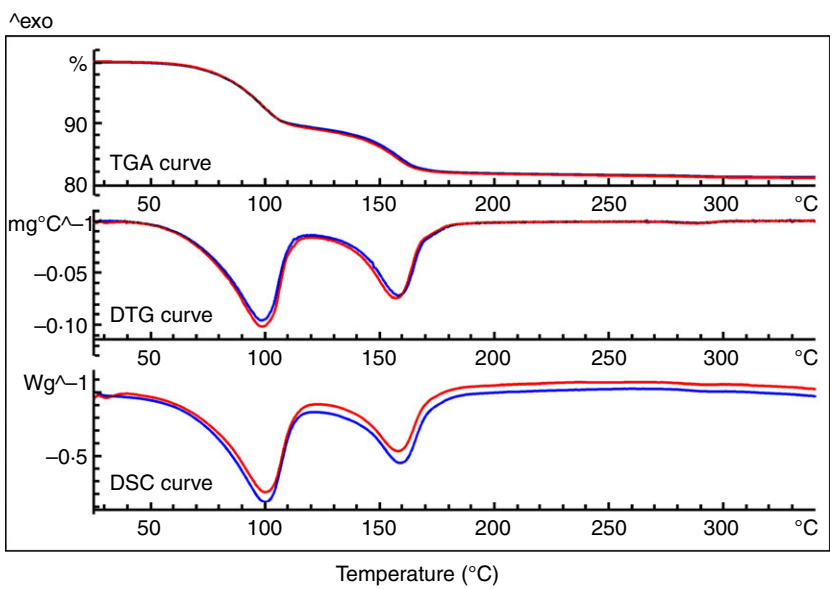

Figure 3 TGA, DTG and DSC curves of the molybdenum trioxide dihydrate $MoO_3 \cdot 2H_2O$, showing the three mass loss steps, as well as the two endothermic process. Similar results obtained under N_2 (blue curves) and under H_2/N_2 (red curves) atmospheres.

Figure 3 shows the results from the thermal analysis (Thermal Gravimetric Analysis (TGA), Thermogravimetric Analysis (DTG), Differential Scanning Calorimetry (DSC)) of MoO_3 dihydrate under nitrogen (red curves) and hydrogen/nitrogen atmosphere (blue curves). Three different stages during thermal dehydration can be identified: (i) one at 95°C, (ii) one from 95 to 155°C (iii) and a third one between 155 and 290°C. The associated mass losses are 11·4 % (97°C), 9·4 % (157°C) and 8·5 % (290°C) and the transition energies, based on the sample mass at the beginning of each process, -312 J g^{-1} (97°C), -165 J g^{-1} (157°C) and -3 J g^{-1} (290°C). TGA

Table 1 Mechanical properties of plasticized cellulose acetate blends (CA-TA) and plasticized cellulose acetate/MoO_3 blends (CA-TA-MoO_3)

Sample	Young's modulus (MPa)	Yield stress (MPa)	Tensile strength (MPa)	Elongation at break (%)
CA-TA	628·8 ± 8·9	31·0 ± 0·5	32·6 ± 0·5	14·4 ± 0·7
CT-TA-Mo	638·9 ± 31·7	32·7 ± 0·5	35·1 ± 0·9	14·6 ± 0·9

curves showed the same weight losses independent of the atmosphere at 340°C. The first three distinct mass loss steps observed by TGA correspond to the losses of physisorbed water, followed by two steps of losing one mole of water per step.

Tensile strength and tensile modulus as well as elongation at break were measured for both samples with and without antimicrobial agent. The results of the tensile tests are shown in Table 1. Young's modulus (E) and elongation at break (ε_B) for the sample with an antimicrobial agent (CA-TA-MoO_3) is slightly higher compared to the sample without antimicrobial particles Cellulose acetate – Triacetine (CA-TA) by 1·6 and 1·4% respectively. Yield stress (σ_y) and ultimate tensile strength (UTS) in CA-TA-MoO_3 blends were higher by 5·5 and 7·7%, respectively, compared to the neat biopolymer blends.

Antimicrobial evaluation shows that molybdenum trioxide-embedded samples (sample CA-TA-MoO_3) exhibit good (elimination after 6 h) to excellent (elimination after 3 h) antimicrobial activities against the three tested bacteria compared to samples without MoO_3 (CA-TA) (Fig. 4). The microbiology test of samples CA-TA-MoO_3 revealed particularly high activities of the molybdenum trioxide particles against *Staph. aureus* and *E. coli* after 3 h while no elimination was observed for sample CA-TA after 12 h. A decrease of the antimicrobial activity against *Ps. aeruginosa* was observed for the samples CA-TA-MoO_3.

The prepared cellulose acetate (CA) samples with embedded MoO_3 particles exhibit an excellent antimicrobial activity. The antimicrobial properties of specimens significantly depend on the morphology of MoO_3 particles on the CA surfaces. Thermal decomposition of the dihydrate to the anhydrous MoO_3 under N_2/H_2 gas leads to a delamination into platelet-like particle shapes by two processes. Firstly, crack initiation by loss of crystallization water with increasing temperature and subsequent crack propagation by the stress from a nonuniform thermal lattice expansion (Sotani 1986; Boudjada *et al.* 1993; Shafaei *et al.* 2016c). As a consequence, the surface area of MoO_3 particles was substantially increased due to the observed delamination. We assume that the lamellar cracks expose additional surface area, which is responsible for the strong increase in the antimicrobial activity of MoO_3. The results

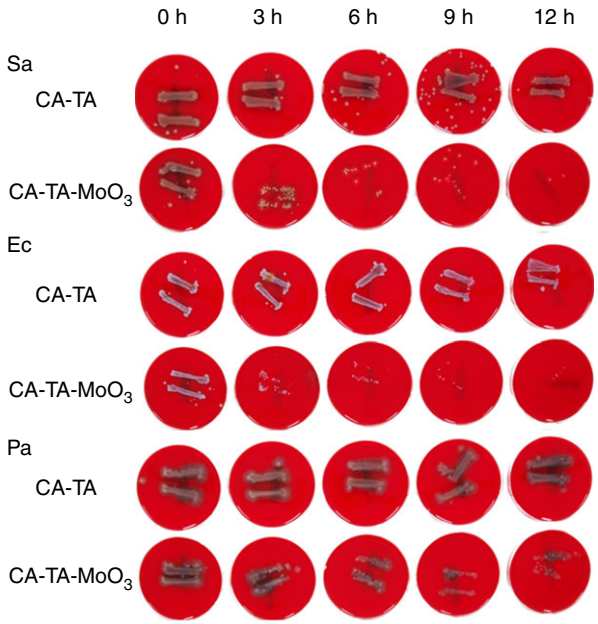

Figure 4 Antimicrobial activities of the anhydrate molybdenum oxides against *Staphylococcus aureus* (Sa) *Escherichia coli* (Ec) and *Pseudomonas aeruginosa* (Pa). CA-TA-MoO_3 eliminated all tested bacteria between 6 and 9 h.

from the DSC and DTG measurements indicated that no reduction of the MoO_3 to MoO_2 occurs during thermal treatment under the H_2/N_2 atmosphere below 340°C. This observation is in accordance with that obtained in literatures (Matsuda *et al.* 2001; Dang *et al.* 2013). The thermally induced lamellar crack formation in MoO_3 supports the proposed mechanism of bacteria elimination by pH values that are locally decreased by proton release from the surface (Zollfrank *et al.* 2012; Shafaei *et al.* 2013b, 2016c). Our results lead the consideration that the combination of a high intrinsic proton release rate and a large surface area is a prerequisite to achieve the desired antimicrobial properties. This characteristic can be realized in our antimicrobial agent, MoO_3. It is required for an efficient antimicrobial activity of the MoO_3 particles on the biopolymer surface that the particles are in contact with water. It is anticipated, that environmental moisture (humidity) would be sufficient to decrease the surface pH value. Uniform dispensation of the MoO_3 particles on the CA surfaces (Fig. 2) after storage under water shows that leaching or dissolution of the MoO_3 from the material surface will only occur at very small amounts and was confirmed by AAS and ICP-OES. This negligible amount indicates the long-lasting durability of antimicrobial agents (as-prepared MoO_3) on the biopolymer surfaces.

In this study, mechanical properties of prepared samples of CA-TA and CA-TA-MoO_3 blends were obtained

by tensile test. As shown in Table 1, Young's modulus and elongation at break were not decreased by adding MoO_3 particles to the CA biopolymer matrix, as one might expect from the addition of filler particles. This might be due to the fact that the inorganic particles exhibit a much higher stiffness values than the soft biopolymer matrix. This can be described by the formation of varied interfacial bonds between molybdenum trioxide particles and CA matrix. This observation is in good agreement with other studies reported in literatures (Fu *et al.* 2008; Chen *et al.* 2013). Yield stress (σ_y) and UTS in CA-TA-MoO_3 blends were slightly higher in comparison to the neat polymer blends. The elevated UTS and σ_y might be related to interfacial bonding and the uniform dispersion of MoO_3 in the polymer matrix facilitating stress transfer between particles and matrix in particle-filled polymer composites as shown by BSE and leaching test. To summarize, the addition of rigid MoO_3 particles to the biopolymer matrix can easily change the modulus which leads to a change in the stiffness of the composite.

We presented a novel material concept to prevent growth of harmful bacteria on biopolymer material surfaces which consists of embedded molybdenum trioxide particles. We confirmed that MoO_3 with unique morphology exhibits a highly efficient antimicrobial activity towards several bacteria such as *Staph. aureus*, *E. coli* and *Ps. aeruginosa*. Plasticized biopolymer (CA) surfaces embedded with as-prepared MoO_3 were virtually free of bacteria within 6 h after incubation with an infectious solution. We could show that the presence of an as-prepared antimicrobial agent (MoO_3) on the biopolymer surface has long-lasting durability under water. The results from mechanical tests demonstrated that adding the antimicrobial agents (MoO_3) into the biopolymer substrates have no negative effect on the strength, elasticity and usability under impeding conditions. It seems that the interfacial bonding has only little effect on the Young's modulus of particulate-filled composition. The antimicrobial activity of MoO_3 is not only related to their surface acidity involving the intermediate formation of molybdic acid but we also find that a large specific surface area of MoO_3 directly increased with antimicrobial activity. We observed crack generation being responsible for the high surface area of MoO_3 which was formed by thermal processes under H_2/N_2 atmospheres at 340°C. This greatly facilitates processing and quality control compared to nanometre-sized antimicrobial particles, making the material suitable for embedding. Our prepared composites based on as-prepared MoO_3 antimicrobial materials are alternative agents to decrease the risk of health care-associated infections, which is one of the most important causes of disease at present. Therefore, this developed composite can be applied for materials used in modern medicine and public environments.

There is an extraordinary broad spectrum of antimicrobial activity of this technology on various surfaces endowed with transition metalloacids, including Gram-positive and Gram-negative micro-organisms irrespective of their resistance against antibiotics, fungi, legionella and virus (Bird flu, swine flu, influenza and hepatitis B virus). The activity also includes the most resistant micro-organisms (CRMos) from recent hospital eruptions. The eradication of micro-organisms is fast, meeting under certain circumstances even the criteria of disinfection. Assessing cell membrane integrity disclosed survival of MRC5 (immortalized mouse lung fibroblasts) cell line.

Materials and methods

Materials

Molybdenum trioxide dihydrate was prepared by adding 50 g of $Na_2MoO_4{\cdot}2H_2O$ (>99·0 %, Fluka, St. Gallen, Switzerland) to 100 ml of water (HiPerSolv Chromanorm, VWR, Darmstadt, Germany) filtered at 0·2 μm and dissolved to 400 ml of 5 mol ml^{-1} HNO_3 (≥99·5 %; Sigma-Aldrich, St. Louis, MO). The solution was stirred at room temperature for 2 h. Precipitation of yellowish particles of molybdenum trioxide started after 1 day and was completed after 3 weeks. The particles were filtered, successively washed with 100 ml of 4 mol ml^{-1} HNO_3, and distilled water, and finally air-dried at room temperature. The as-synthesized material $MoO_3{\cdot}nH_2O$ was further calcined in a 4 vol.-% H_2 and 96 vol.-% N_2 atmosphere at 340°C at a heating rate of 5°C min^{-1} for 2 h. The biopolymer matrix consisted of a commercial grade CA with $M_w = 5{\cdot}0 \times 10^4$ and a degree of substitution (DS) of 2·5 (Eastman Chemical Company, CA-398-30, Kingsport, TN). Sample CA-TA was prepared by adding 12·9 g triacetine (Cognis Oleochemical, Edenor GTA, Selangor, Malaysia) as a plasticizer to 28·1 g CA. The mixture was stirred with a mechanical stirrer at room temperature for 30 min. CA and MoO_3 were dried under vacuum at 80°C for 24 h before use. Sample CA-TA-MoO_3 was prepared by first dispersing 0·62 g of the as-prepared MoO_3 powder in 28·1 g CA. Subsequently, 12·2 g of triacetine was added slowly to the dispersion of CA and MoO_3 and mixed with a mechanical stirrer at room temperature for 30 min.

Methods

A laboratory extruder (HAAKE Minilab II; Thermo Fisher, Karlsruhe, Germany) equipped with a conical twin-screw was used for the compounding process. The

composites consisting of cellulose acetate, triacetine and as-prepared molybdenum trioxide were extruded through a slit die (5 mm × 0·5 mm) to yield sheets for antimicrobial test. To obtain specimens for tensile testing, composite materials were transferred to a laboratory-scale injection moulding machine (HAAKE Mini-jet; Thermo Electron GmbH, Karlsruhe, Germany) at 180°C and 700 bar. The dumbbell-shaped specimens had dimensions of 75 × 5 × 2 mm. Part of the samples were stored in double distilled water for 2 months for the determination of a possible dissolution of the MoO_3 particles. The mother liquids were kept for the determination of the Mo content.

The antimicrobial properties of the composite materials were investigated with respect to *Staph. aureus* ATCC 25923 (MRSA), *E. coli* ATCC 27020 and *Ps. aeruginosa* ATCC 10145 using the roll-on test, which was already shown to be highly sensitive for materials surfaces (Maki *et al.* 1977; Samuel and Guggenbichler 2004). The specimens (sample rod) are incubated in an inoculum (10^7–10^9 CFU ml^{-1}) with reference bacteria for 4 h. This time is sufficient for the bacteria to colonize the surface of the sample and to induce the formation of a biofilm. The specimen is removed from the inoculum, adhering droplets are gently removed and the specimen is rolled over a Columbia agar plate (OXOID TSB) with the addition of 5% defibrinated sheep blood. The specimen is then placed in a sterile 0·25 mol ml^{-1} saline. The roll-on step is repeated on a fresh agar plate every 3 h. After incubation at 37°C for 24 h, the bacterial growth on the agar plates is consecutively monitored.

SEM (DSM 940A; Zeiss, Oberkochen, Germany) was used to acquire micrographs of the MoO_3 samples at an acceleration voltage of 25 kV. The samples were sputter-coated with gold prior to SEM examination. BSE microscopy was used to determine durability of antibacterial particles on the biopolymer surface before and after storage under water for 2 months.

The mother liquids from the leakage experiment were investigated by AAS (ZEEnit 700; Analytik Jena AG, Jena, Germany) and inductively coupled plasma optical emission spectrometry (ICP-OES, Spectroflame Modular; Spectro Analytical Instruments Inc., Kleve, Germany).

The phase transition of molybdenum trioxide and the total content of water of crystallization were obtained by differential scanning calorimetry and differential thermal analysis (TGA/DSC 2; STAR^e System, METTLER TOLEDO, Schwerzenbach, Switzerland).

Specific surface area analysis was carried out by nitrogen physisorption (Nova 4000e; Quantachrome, Odelzhausen, Germany). Specific surface areas were calculated using 5-point Braunauer–Emmet–Teller (BET) plots in the range of 0·1–0·3 bar relative pressure at 77 K. All samples were degassed at 25–50 °C for 24 h prior to measurement.

Uniaxial tensile testing was carried out according to ISO 527-2-A5 standard with a tensile testing system (smarTens, Karg Industrietechnik, Krailling, Germany). The applied strain rate was 10 mm min^{-1}, and the sample was deformed to 8 mm until failure. The equilibrium stress–strain relationship of the material was recorded and the elastic modulus was calculated from the linear part of the stress–strain curve.

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Conflict of Interest

The authors have no conflict of interest to declare.

References

Bao, T., Yin, W., Zheng, X., Zhang, X., Yu, J., Dong, X., Yong, Y., Gao, F. *et al.* (2016) One-pot synthesis of PEGylated plasmonic MoO_{3-x} hollow nanospheres for photoacoustic imaging guided chemo-photothermal combinational therapy of cancer. *Biomaterials* **76**, 11–24.

Barceloux, D.G. (1999) Molybdenum. *J Toxicol Clin Toxicol* **37**, 231–237.

Bechert, T., Steinrücke, P. and Guggenbichler, J.P. (2000) A new method for screening anti-infective biomaterials. *Nat Med* **6**, 1053–1056.

Boll, M., Schink, B., Messerschmidt, A. and Kroneck, P.M.H. (2005) Novel bacterial molybdenum and tungsten enzymes: three dimensional structure, spectroscopy and reaction mechanism. *Biol Chem* **386**, 999–2006.

Boudjada, N., Rodriguez-Carvajal, J., Anne, M. and Figlarz, M. (1993) Dehydration of $MoO_3 \times 2H_2O$: a neutron thermosdiffractometry study. *J Solid State Chem* **105**, 211–222.

Chen, J., Kinloch, A.J., Sprenger, S. and Taylor, A.C. (2013) The mechanical properties and toughening mechanisms of an epoxy polymer modified with polysiloxane-based core-shell particles. *Polymer* **54**, 4276–4289.

Dang, J., Zhang, G.H. and Chou, K.C. (2013) Phase transition and morphology evolutions during hydrogen reduction of MoO_3 to MoO_2. *High Temp Mater Proc* **33**, 305–312.

Das, D., Nath, B.C., Phukon, P. and Dolu, S.K. (2013) Synthesis and evaluation of antioxidant and antibacterial

behavior of CuO nanoparticles. *Colloids Surf B Biointerfaces* **101**, 430–433.

Delgado, K., Quijada, R., Palma, R. and Palza, H. (2011) Polypropylene with embedded copper metal or copper oxide nanoparticles as a novel plastic antimicrobial agent. *Lett Appl Microbiol* **53**, 50–54.

Fakhri, A. and Nejad, P.A. (2016) Antimicrobial, antioxidant and cytotoxic effect of molybdenum trioxide nanoparticles and application of this for degradation of ketamine under different light illumination. *J Photochem Photobiol, B* **159**, 211–217.

Fu, S.Y., Feng, X.Q., Lauke, B. and Mai, Y.W. (2008) Effects of particle size, particle/matrix interface adhesion and particle loading on mechanical properties of particulate–polymer composites. *Composites Part B* **39**, 933–961.

Gorman, S.P. and Jones, D.S. (2002) Antimicrobial biomaterials for medical devices. World markets research center. *Med Device Manuf Technol*, 97–101.

Guggenbichler, J.P., Eberhardt, N., Martinez, H.P. and Wildner, H. (2010). Substance with an antimicrobial effect. US20100057199.

Gupta, U.C. and Gupta, S.C. (1998) Trace element toxicity relationships to crop production and livestock and human health: implications for management. *Commun Soil Sci Plant Anal* **29**, 1491–1522.

Gutbrod, K. and Zollfrank, C. (2013) The photocataytic properties of Ti-Mo oxides prepared by a simple sol-gel route. *J Sol-Gel Sci Technol* **66**, 111–119.

Hänzelmann, P. and Schindelin, H. (2004) Crystal structure of the S-adenosylmethionine-dependent enzyme MoaA and its implications for molybdenum cofactor deficiency in humans. *Proc Natl Acad Sci USA* **31**, 12870–12875.

Hazer, D.B., Burcu, D., Mut, M., Dincer, N., Saribas, Z., Hazer, B. and Ozgen, T. (2012) The efficacy of silver embedded polypropylene-grafted polyethylene glycol-coated ventricular catheters on prevention of shunt catheter infection in rats. *Childs Nerv Syst* **28**, 839–846.

Heijerick, D.G., Regoli, L. and Stubblefield, W. (2012) The chronic toxicity of molybdate to marine organisms. I. Generating reliable effects data. *Sci Total Environ* **430**, 260–269.

Kalaycı, O.A., Comert, F.B., Hazer, B., Atalay, T., Cavicchi, K.A. and Cakmak, M. (2010) Synthesis, characterization, and antibacterial activity of metal nanoparticles embedded into amphiphilic comb-type graft copolymers. *Polym Bull* **5**, 215–226.

Kapp, R. (2005) Molybdenum. *Environ Toxicol* **3**, 145–148.

Kirk, M.L. and Stein, B. (2013) Molybdenum enzymes. In *Comprehensive Inorganic Chemistry II* eds. Reedijk J. and Poeppelmeier K.R. Vol. 3, pp. 263–293. Amsterdam, Netherlands: Elsevier

Klevens, R.M., Edwards, J.R., Richards, C.L. Jr, Horan, T., Gaynes, R.P., Pollock, D.A. and Cardo, D.M. (2007) Estimating health care-associated infections and deaths in U.S. hospitals, 2002. *Public Health Rep* **122**, 160–166.

Krishnamoorthy, K., Veerapandian, M., Yun, K. and Kim, S.J. (2013a) New function of molybdenum trioxide nanoplates: toxicity towards pathogenic bacteria through membrane stress. *Colloids Surf B Biointerfaces* **112**, 521–524.

Krishnamoorthy, K., Premanathan, M., Veerapandian, M. and Kim, S.J. (2014b) Nanostructured molybdenum oxide-based antibacterial paint: effective growth inhibition of various pathogenic bacteria. *Nanotechnology* **25**, 315110.

Lackner, M. and Guggenbichler, J.P. (2013a) Antimicrobial surfaces. *Ullmann's Encyclopedia of Industrial Chemistry* ed. Elvers B. pp. 1–13. Weinheim: Wiley-VCH Verlag.

Lackner, M. and Guggenbichler, J.P. (2013b) Composition with at least one antimicrobial agent. German Patent: DE102011085862.

Lackner, M. and Guggenbichler, J.P. (2013c) Composite material comprising a support material and an antimicrobial agent. German Patent: DE102012103064.

Lackner, M., Maninger, S. and Guggenbichler, J.P. (2013) Saure Oberflächen als neuartige Kontaktbiozide. *Nachr Chem* **61**, 112–115.

Levina, A., Mc Leod, A.I., Seuring, J. and Lay, P.A. (2007) Reactivity of potential anti-diabetic molybdenum (VI) complexes in biological media: a XANES spectroscopic study. *J Inorg Biochem* **101**, 1586–1593.

Lorenz, K., Bauer, S., Gutbrod, K., Guggenbichler, J.P., Schmuki, P. and Zollfrank, C. (2011) Anodic TiO_2 nanotube layers electrochemically filled with MoO_3 and their antimicrobial properties. *Biointerphases* **6**, 16–21.

Magill, S.S., Edwards, J.R., Bamberg, W., Beldavs, G.Z., Dumyati, G., Kainer, M.A., Lynfield, R., Maloney, M. *et al.* (2014) Multistate point-prevalence survey of health care–associated infections. *N Engl J Med* **370**, 1198–1208.

Maki, D.G., Jarrett, F. and Sarafin, H.W. (1977) A semiquantitative culture method for identification of catheter-related infection in the burn patient. *J Surg Res* **22**, 513–520.

Mardare, C.C. and Hassel, A.W. (2014) Investigations on bactericidal properties of molybdenum – tungsten oxides combinatorial thin film material libraries. *ACS Comb Sci* **16**, 631–639.

Matsuda, T., Hirata, Y., Itoh, H., Sakagami, H. and Takahashi, N. (2001) Effect of reduction temperature on the transformation of MoO_3 to MoO_x with a large surface area. *Microporous Mesoporous Mater* **42**, 337–344.

Raghupathi, K.R., Koodali, R.T. and Manna, A.C. (2011) Size-dependent bacterial growth inhibition and mechanism of antibacterial activity of zinc oxide nanoparticles. *Langmuir* **27**, 4020–4028.

Repetto, L., Comandini, D. and Mammoliti, S. (2001) Life expectancy, comorbidity and quality of life: the treatment equation in the older cancer patients. *Crit Rev Oncol Hematol* **37**, 147–152.

Ribeiro, A.M., Flores-Sahagun, H.S.T. and Paredes, R.C. (2016) A perspective on molybdenum biocompatibility and antimicrobial activity for applications in implants. *J Mater Sci* **51**, 2806–2816.

Rodríguez, F.J., Torres, A., Peñaloza, Á., Sepúlveda, H., Galotto, M.J., Guarda, A. and Bruna, J. (2014) Development of an antimicrobial material based on a nanocomposite cellulose acetate film for active food packaging. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* **31**, 342–353.

Samuel, U. and Guggenbichler, J.P. (2004) Prevention of catheter-related infections: the potential of a new nano-silver impregnated catheter. *Int J Antimicrob Agents* **23**, 75–78.

Shafaei, S., Lackner, M., Meier, M., Plank, J., Guggenbichler, J.P. and Zollfrank, C. (2013b) Polymorphs of molybdenum trioxide as innovative antimicrobial materials. *Surf Innovations* **1**, 202–208.

Shafaei, S., Lackner, M., Voloshchuck, R., Voloshchuck, I., Guggenbichler, J.P. and Zollfrank, C. (2014a) Innovative development in antimicrobial inorganic materials. *Recent Patents Mater Sci* **7**, 26–36.

Shafaei, S., Opdenbosch, D.V., Fey, T., Koch, M., Kraus, T., Guggenbichler, J.P. and Zollfrank, C. (2016c) Enhancement of the antimicrobial properties of orthorhombic molybdenum trioxide by thermal induced fracturing of the hydrates. *Mater Sci Eng, C* **58**, 1064–1070.

Sotani, N. (1986) Structural and compositional changes in a hydrogen molybdenum bronze, $H_{0.83}MoO_3$, by vacuum heating. *Polyhedron* **5**, 67–69.

Tétault, N., Gbaguidi-Haore, H., Bertrand, X., Quentin, R. and Vander, M.M.N. (2012) Biocidal activity of metalloacid-coated surfaces against multidrug-resistant microorganisms. *Antimicrob Resist Infect Control* **1**, 35–41.

Tran, T.A., Krishnamoorthy, K., Song, Y.W., Cho, S.K. and Kim, S.J. (2014) Toxicity of nano molybdenum trioxide toward invasive breast cancer cells. *ACS Appl Mater Interfaces* **6**, 2980–2986.

Treacy, P.J. and Goldberg, D.J. (2006) Use of a biopolymer polyalkylimide filler for facial lipodystrophy in HIV-positive patients undergoing treatment with antiretroviral drugs. *Dermatol Surg* **6**, 804–808.

Vieira, M.G.A., Silva, M.A.D., Santos, L.D. and Beppu, M.M. (2011) Natural-based plasticizers and biopolymer films. *Eur Polym J* **48**, 254–263.

Wuebbens, M.M., Liu, M.T., Rajagopalan, K. and Schindelin, H. (2000) Insights into molybdenum cofactor deficiency provided by the crystal structure of the molybdenum cofactor biosynthesis protein MoaC. *Structure* **8**, 709–718.

Zollfrank, C., Gutbrod, K., Wechsler, P. and Guggenbichler, J.P. (2012) Antimicrobial activity of transition metal acid MoO_3 prevents microbial growth on material surfaces. *Mater Sci Eng, C* **32**, 47–54.