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Development and industrial implementation of a biodegradable surgical wire production technology from ZnMg0.004 alloy: *In vitro* assessment of degradation rate and mechanical property changes

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Abstract. The paper discusses the technology for the production of the new biodegradable surgical wire, developed at AGH, along with the experience of its integration into INTERMECH's production processes. This wire's basic mechanical and corrosion properties are thoroughly examined. The developed technology is based on the use of a combination of hot and cold (in the last passes) drawing of a workpiece obtained by hot extrusion. Hot drawing allows to achieve the necessary ductility of the wire, while the final cold drawing improves the surface quality, which is important in the context of the biological properties of the wire. To assess biodegradation rates, *in vitro* testing was conducted within a natural corrosive environment (using bovine serum from Biowest). Mechanical tensile tests were performed on wires at various stages of corrosion, ranging from 3 to 30 days, in addition to the original wire. These tests were carried out using a Zwick 250 testing machine. The study revealed that the tensile strength of all produced wires decreases by less than 50% after 30 days of corrosion. Further experimental investigations were conducted to monitor changes in wire mass over time. The tests spanned 120 days, during which the corrosion rate declined from 2 mm/year in the initial days to approximately 0.05 mm/year in the later stages. This study indicates that when planning the use of this wire in bone surgery, a corrosion time of 1-2 years should be anticipated. In cases where the wire is exposed to intense bodily fluid flushing, this timeline may be shorter.

Introduction

The first use of metallic biodegradable surgical sutures dates back to the mid-19th century [1], employing pure magnesium and later its alloys [2]. The expectation was that these threads, with mechanical properties anticipated to surpass those of polymer threads, would address issues like reoperation (the subsequent removal of threads) and provide mechanical unloading to healing tissues during biodegradation. However, challenges such as excessive corrosion rates, hydrogen release during corrosion, and inadequate ductility of wires made from magnesium alloys when tying different surgical knots prompted a quest for alternative biodegradable metals and alloys.

A potential solution emerged with the usage of zinc alloys containing a small amount (up to 0.1% by weight) of magnesium [3]. The objective of this alloying was to enhance the mechanical properties of zinc to a level suitable for manufacturing biodegradable implants.

Biodegradable polymer-based sutures for soft tissue joining are prevalent in the market. A comparison of the mechanical properties between these threads and those made from magnesium alloys and zinc is detailed in [4]. Specifically, the study reveals that, under the influence of a surgical knot, both magnesium alloy wires and conventional polymer sutures experience approximately a 50% reduction in tensile strength. Contrastingly, zinc wire, subject to the same knot, exhibits only a 3% decrease in strength.

Surgical steel wire is the current standard for connecting hard tissues, such as bone fragments post-fracture. However, there is a lack of biodegradable alternatives in the market. Addressing this gap, [5] focuses on studying the production of biodegradable surgical wire for hard tissue connection. In [6], a laboratory-developed technology for manufacturing such wires from Zn-Mg alloys is presented. This process involves ingot production, extrusion, and hot and cold drawing, resulting in wire diameters ranging from 0.3 to 1 mm.

Paper [7] delves into the biological properties of the produced wire, determining the optimal magnesium content in zinc, leading to high cell viability, particularly with osteoblasts. This finding highlights the suitability of the ZnMg0.004 alloy as the primary material for biodegradable surgical wire production.

The technology was subsequently implemented at INTERMECH Sp. z o.o., focusing on producing biodegradable surgical wire for veterinary medicine.

This study aims to assess changes in the mechanical properties of wires under industrial production conditions, considering time and the degree of biocorrosion *in vitro*. These results hold significance both in the scientific realm and as practical insights for surgeons

Material and Methods

The work examines the ZnMg0.004 alloy, which has the following chemical composition (in wt. %): Mg 0.0034wt.%; Pb < 0.003 wt.%; Cd < 0.003 wt.%; Fe < 0.002 wt.%; Sn < 0.001 wt.%; Cu < 0.001 wt.%; Al < 0.001wt.%; Zn – balance.

A detailed description of the production process for ZnMg0.004 alloy is present below.

- Alloy formation: The process begins with the creation of the zinc-magnesium alloy by introducing magnesium into molten zinc using an induction furnace. This fusion results in the formation of the alloy.

- Ingot casting. The alloy is then cast into ingots with a diameter of 120 mm. These ingots serve as the initial material for further processing.

- Ingot cutting. Following casting, the ingots are precisely cut into billets, each with a height of 160 mm. This step prepares the alloy for subsequent processing stages.

- Chemical composition control: To ensure the alloy's chemical composition, the atomic absorption spectroscopy (AAS) method is employed for meticulous quality control.

- Extrusion. This production phase involves extruding the billet through a die with 30 channels, each having a diameter of 1.8 mm.

- Hot drawing (Fig 1, position 1): The extruded material is subjected to hot drawing, which commences at a temperature within the deformation zone ranging from 150 to 200°C. This process reduces the wire's diameter to 1.3 mm. The drawing speed is set at 10 mm/s.

- Cold drawing (Fig. 1, position 2): Subsequent drawing continues at room temperature, further reducing the wire's diameter from 1.3 mm to its final size of 0.8-1.0 mm.

- Cleaning process. During the drawing process, meticulous cleaning is carried out to maintain the wire's surface purity. The wire is carefully wiped with cotton wool and ethanol to eliminate any foreign substances that could potentially affect cytotoxicity.

- Ultrasonic cleaning (Fig. 1, position 4). At the penultimate stage, the wire undergoes an additional cleaning step, where it is immersed in an ultrasonic bath filled with water and a small quantity of liquid soap. This ensures the removal of any residual impurities.

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- Final rinse: The wire is finally rinsed for 15 minutes in a solution of 70% alcohol, further enhancing its cleanliness and suitability for biomedical applications.

- Mechanical testing of the final wires in the manufacturing process can be performed in dedicated equipment (Fig. 1, position 5).

Fig. 1. Industrial technological line (INTERMECH Sp. z o.o.): 1 – the device for hot drawing; 2 – the device for cold drawing; 3 - the control electronic system; 4 – devices for ultrasonic cleaning; 5 - mechanical testing machine of the final wires.

Wire samples, post-production, underwent *in vitro* corrosion under laboratory conditions for varying durations: 3, 7, 14, 21, and 28 days. The wire ends were insulated against corrosion (Fig. 2) to facilitate mounting in a Zwick250 machine, used for mechanical tensile tests. These tests were conducted at room temperature with a deformation velocity of 20 mm/min. Fig. 3 illustrates samples before and after 28 days of corrosion. Three samples were used for each corrosion period to assess result accuracy.

The *in vitro* corrosion tests were performed in a mixture of bovine serum supplied by Biowest (catalog No. S0250, https://www.biowest.net. Accessed 2 Dec 2019). The protein content in the mixture was equal to 30 g/l. Sodium azide (0.3 wt%) and 20 mM of ethylenediaminetetraacetic acid were added to the solution to inhibit bacteria growth and bind calcium ions. The mixture was filtered through a sterile filter (pore size 20 μm). During corrosion tests, the pH value and the temperature of the corrosion medium were kept equal to 7.2–7.4 and 37 ± 0.1 °C, respectively. The protein concentration was monitored by a Genesys™20 spectrophotometer (Spectronic Instruments, USA). During the *in vitro* corrosion test all recommendations given by the ASTM F732-00 standard were satisfied.

Additionally, studies of changes in the mass of the samples over a period of up to 120 days were carried out on individual samples approximately 100 mm long. After each test period, the samples were removed from the corrosion medium and a change in their weight was determined using a laboratory balance with an accuracy of 0.00001 g.

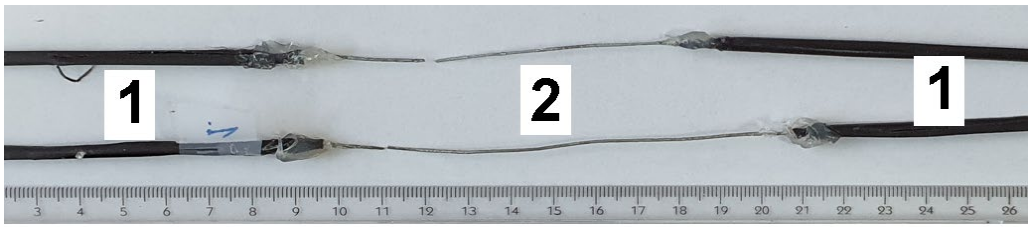


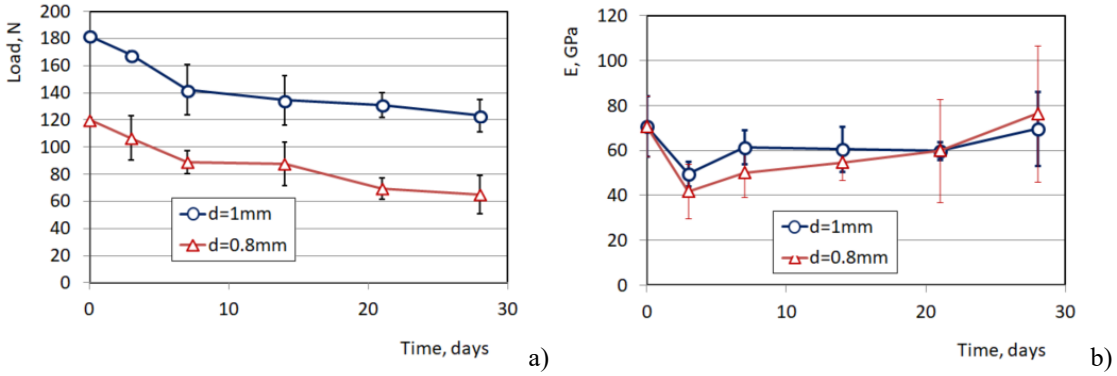
Fig. 2. Photos of samples after corrosion and strength tests: 1 – fragments of the sample, isolated from the corrosive medium; 2 – working part of the sample.

Fig. 3. Wire with an initial diameter of 1 mm before (top image) and after 28 days of corrosion (bottom image).

Results

The main research results are presented in Fig. 4. The change in the maximum force corresponding to wire rupture depending on the corrosion time is shown in Fig. 4,a. It follows from it that the decrease in wire strength over a month of corrosion was 33% and 47% for wire with an initial diameter of 1 and 0.8 mm, respectively. No statistically significant changes in the mechanical properties of the wire material (Young's modulus and tensile strength, Fig. 4,b and 4,c, respectively) were recorded. For these parameters, an increase in the measurement error is observed, which is associated with an increase in the measurement error of the wire diameter after corrosion, which becomes more uneven along the length than for the original wire (Fig. 3).

For the period corresponding to the time of corrosion of the samples before mechanical tests, the change in the mass of the samples is shown in Fig. 4,d. It follows from this that corrosion occurs most intensely in the first two weeks of the process. The total time of such tests was 120 days. During this period, the corrosion rate for wires with an initial diameter of 1.0 mm ranged from 2.3 mm/year in the initial 3 days to 0.19 mm/year after 28 days, decreasing to approximately 0.05 mm/year in the later stages. For wires with an initial diameter of 0.8 mm, these values were 2.17, 0.30, and 0.05 mm/year, respectively. Examples of SEM images depicting wires at different stages of corrosion are presented in Fig. 5. Ultimately, this study suggests that a full degradation time of 1-2 years should be expected. However, it's important to exercise caution in interpreting this assessment, as the rate of corrosion *in vitro* may significantly differ from that *in vivo*. A more accurate estimation of the time required for complete wire dissolution will be attainable upon completion of the entire cycle of clinical trials.



a) b)

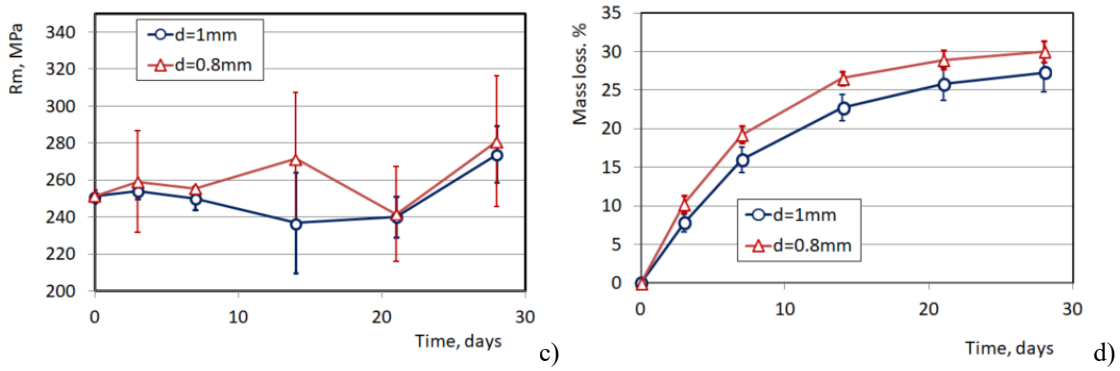


Fig. 4. Result of the mechanical tests of the ZnMg0.004 wire after corrosion (a, b, c) and mass loss of the wire during corrosion (d).

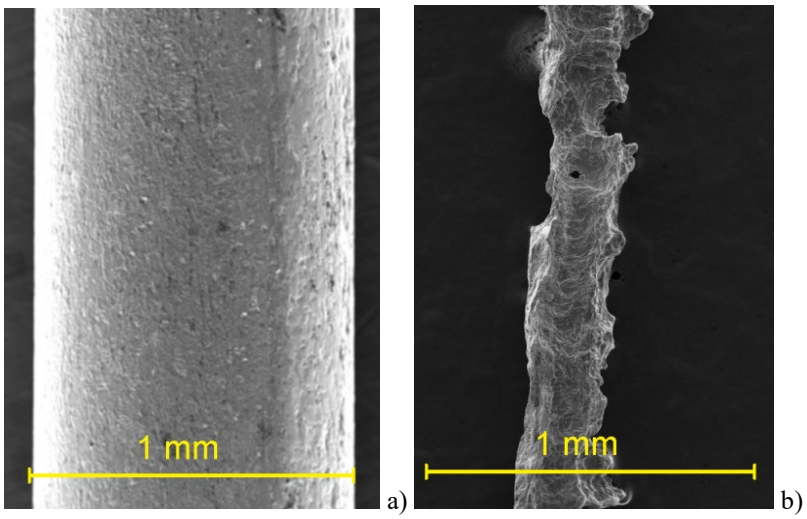


Fig. 5. SEM images of wire with an initial diameter of 1 mm made from ZnMg0.004 alloy after initial (a) and final stage (b) of corrosion in vitro.

Discussion

Of significant practical interest is the relationship between the maximum wire-breaking force and the amount of wire mass loss during corrosion. A representation of the experimental data in such coordinates is shown in Fig. 6a. Approximation of the obtained dependence using linear functions showed a high R^2 coefficient (R-squared coefficient of determination). This fact is a consequence of fairly uniform corrosion of the wire over its surface. As follows from the images in Fig. 5, even at the last stages of corrosion, wire made of ZnMg0.004 alloy does not lose continuity. In practice, the equations shown in Fig. 6a make it possible to predict changes in wire strength depending on mass loss due to corrosion. The obtained conclusion makes it possible to evaluate the loss of wire strength if there is only a curve for the change in wire mass during corrosion and to avoid repeating long and expensive mechanical tests of the material after various stages of corrosion.

It is also of interest to answer the question of whether this pattern holds for all materials. To find the answer, we will use a similar study of the strength of wires with an initial diameter of 1.8 mm from the MgCa0.9 and MgCa1.2 alloys after corrosion in the same corrosive environment [8]. Similar to Fig. 6a, we present the change in wire strength as a result of *in vitro* corrosion as a dependence of the breaking force on the loss of wire mass. The obtained dependences (Fig. 6b) are characterized by a much lower value of the R-squared coefficient of determination than in the case of the ZnMg0.004 alloy considered in this work. The reason for this difference is that the

corrosion of magnesium alloys is more uneven over the surface of the wire than of zinc and its alloys.

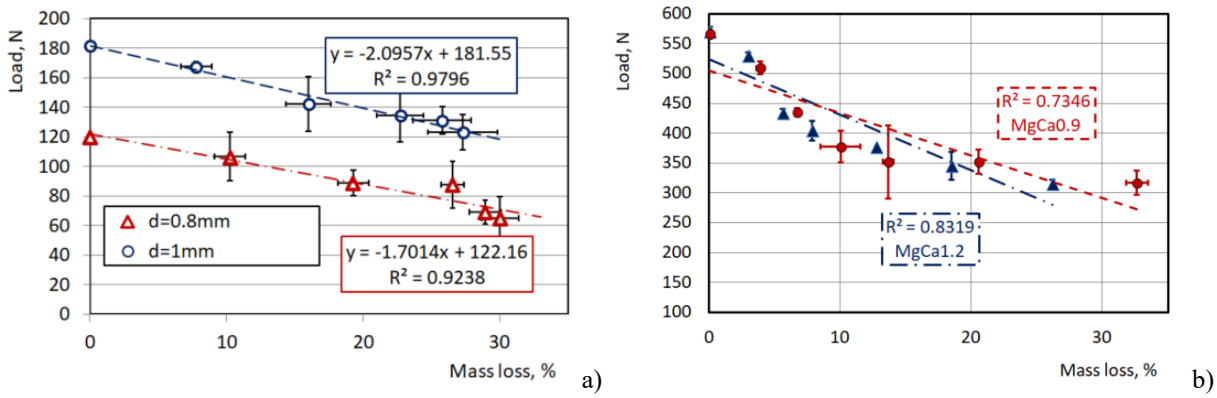


Fig. 6. Relationship between the ultimate load of wire and mass loss during corrosion: a – for ZnMg0.004 alloy; b – for MgCa alloys.

Summary

Biodegradable surgical wires with diameters of 0.8 and 1.0 mm, manufactured at INTERMECH from the ZnMg0.004 alloy, were investigated.

Based on strength tests after different stages of corrosion, it was found that the decrease in strength (breaking force) of the tested wires after 28 days of *in vitro* corrosion is less than 50% of their initial strength.

For the *in vitro* corrosion conditions tested, it was found that the decrease in wire strength is linearly proportional to the wire mass loss during corrosion, which is the result of uniform corrosion on the wire surface. Analogous tests for Mg-Ca alloys showed the lack of such proportionality due to the different nature of corrosion of Mg-Ca and Zn-Mg alloys.

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