Polymer composites for medical applications as artificial bones

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Abstract: Polymer composites based on epoxy resin (EP) were developed from which anatomical models of artificial cortical bone tissue were obtained. The cancellous bone was polyurethane foam. To obtain appropriate mechanical properties, the EP was filled with $CaCO_3$ (50, 60, 70 wt%) and a hybrid filler in the form of a mixture of silica and perlite (3/3, 5/5, 7/7 wt%/wt%). Samples for mechanical testing were obtained by vacuum casting in silicone molds. The influence of the type and amount of filler on the mechanical properties of the composite was demonstrated. $CaCO_3$ had a particularly beneficial effect on hardness, compressive stress, and Young's modulus. The obtained anatomical bone model did not differ from natural bone in terms of structure and properties. This type of implants can be used in orthopedics and veterinary medicine.

Keywords: artificial bone, polymer composites, materials used in medicine, fillers, mechanical properties.

Kompozyty polimerowe do zastosowań medycznych jako sztuczne kości

Streszczenie: Opracowano kompozyty polimerowe na bazie żywicy epoksydowej (EP), z których uzyskano modele anatomiczne sztucznej korowej tkanki kostnej. Kością gąbczastą była pianka poliuretanowa. W celu uzyskania odpowiednich właściwości mechanicznych EP napełniono $CaCO_3$ (50, 60, 70% mas.) oraz napełniaczem hybrydowym w postaci mieszaniny krzemionki z perlitem (3/3, 5/5, 7/7 %mas./%mas.). Próbki do badań mechanicznych otrzymano metodą odlewania próżniowego w formach silikonowych. Wykazano wpływ rodzaju i ilości napełniacza na właściwości mechaniczne kompozytu. Szczególnie korzystny wpływ na twardość, naprężenie ściskające i moduł Young'a miał $CaCO_3$. Otrzymany model anatomiczny kości pod względem struktury i właściwości nie odbiegał od naturalnej kości. Tego typu implanty mogą znaleźć zastosowanie w ortopedii i weterynarii.

Słowa kluczowe: sztuczna kość, kompozyty polimerowe, materiały stosowane w medycynie, napełniacze, właściwości mechaniczne.

The first polymeric materials used for biomedical applications were naturally occurring polymers. Their place was replaced by synthetic polymers in the 1960s. Currently, both types of these materials are used in medicine. The high compatibility of natural polymers is their great advantage, which is why they are so willingly used in regenerative medicine, but their disadvantages include the possibility of triggering an unwanted immune response by the body. This process is prevented using materials made of synthetic polymers, which are also often used due to their easy reproduction, longer shelf life and the possibility of modifying the structure depending on the purpose of use [1–7].

Polymer materials are used in many industries. Modern techniques, e.g., 3D printing, are used in various fields of medicine, such as tissue engineering, drug delivery systems, production of laboratory equipment and auxiliary tools, prostheses, orthoses, and implants. In the 1980s, this method initiated a huge development in medicine, especially implantology. Because of this technique, medical devices supporting the planning and performance of surgeries, models for academic and clinical teaching, as well as prototypes of tissues and organs are produced [8, 9]. In medicine, polymer materials are used in craniofacial and spine surgery, neurology, cardiovascular surgery, as well as for transplantation of entire organs, including synthetic bones. The use of polymers to produce bone imitations provides wide opportunities for the development of implantology. There are also various methods of applying polymers in implants and medical

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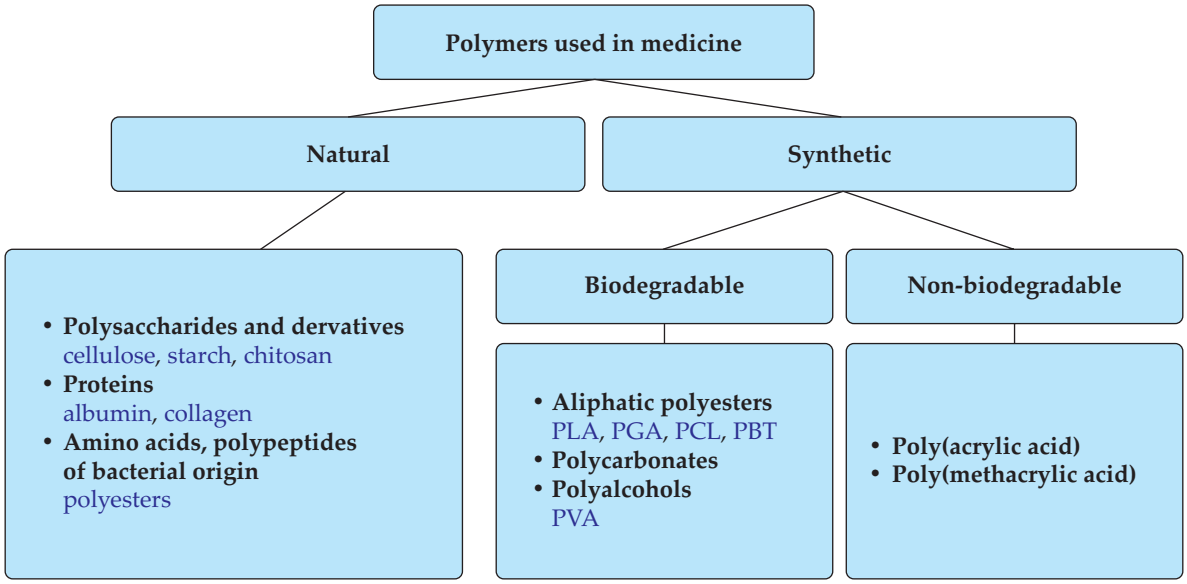

Fig. 1. Polymer materials used in medicine [11]

devices, e.g., in the form of a protective coating, an adhesive, or a substrate for the device [10].

Regenerative medicine eagerly uses the vacuum casting process, which is a cheap and quick method of reproducing selected products in small series. The vacuum casting method in silicone molds uses cheaper tools and materials, so it is a good alternative to existing micro mold production methods. Moreover, the silicone rubber used to produce molds is characterized by good thermal stability and chemical resistance, which allows casting from a wide range of resins. This material is composed of Si-O and Si-C chains contained in a matrix of linear polymers, which allows free exchange of molecules and low interfacial energy. Therefore, the cast material is not exposed to reaction with the mold surface [4–6, 12–14].

To obtain subsequent parts by vacuum casting, chemically cured resins such as polyester, polyurethane or epoxy resins are used. Specific functional or aesthetic properties of castings are obtained by mixing resin with fillers. They can be both coloring pigments that give the product aesthetic value, as well as silica or metal powders that influence the final physicochemical properties of the product [4, 5]. Currently, there is an increase in interest in hybrid composites, and their appropriate design allows the use of the features of individual components. This results in minimizing the disadvantages resulting from their individual use [6].

The function of bones is primarily to stabilize the body and protect internal organs. The skeleton is a scaffold to which the muscles are attached, which is why it is one of the most important parts of the body. Bone is a specific form of connective tissue consisting of collagen fibers and calcium and phosphorus salts. Bone tissue is constantly resorbed and replaced by new tissue. This process ensures bone reconstruction by removing the resulting defects. Bones are the largest store of calcium ions, 99% of this element is found in bone tissue [15]. Other trace elements responsible for the proper functioning of the body are also present. The mineral elements that make up bone tissue are calcium, magnesium, silicon, phosphorus, and zinc. In the field of bone regenerative engineering, numerous studies are being conducted to find appropriate synthetic materials that will allow not only the reconstruction and regeneration of bones, but also the creation of entire implants [16].

Modern biomaterials should be distinguished primarily by non-toxicity, biocompatibility, bioactivity, and corrosion resistance [16, 17]. The material that meets these conditions is hydroxyapatite, which has become one of the best implantation materials. It is classified as a ceramic material and its structure is based on calcium phosphates. Biological appetites are inorganic components of bones and teeth, which is why they are widely used in medicine [17–19]. In addition to calcium phosphates, the most common biomaterials in nature include calcium carbonate ($CaCO_3$) used in bone regenerative medicine. It has been considered a potential precursor for inducing the formation of bone minerals. Its biocompatibility offers a wide range of applications in surgery [20, 21]. Calcium carbonate occurs in a hydrated form and is characterized by high solubility and plasticity but does not have a fixed crystal structure [22]. It constitutes about 4% of the composition of the Earth's crust. It is a basic component of bones and teeth and many rocks, and is also found in crustacean skeletons, shells, corals, and pearls. It is used in many industries, including in construction, medicine, cosmetics, and a newly developing field - biomineralization [23]. The features of $CaCO_3$ such as non-toxicity and porosity allow for wide use in tissue engineering and bone reconstruction. The total calcium content in the human body is 1.5% of body weight, and most of it is found in bones in the form of apatite's. Calcium participates in hormonal

regulation, performs structural functions, and participates in the regulation of homeostasis [24].

Currently, many studies use silica and perlite in hybrid systems. Silica is characterized by high thermal and chemical resistance, as well as susceptibility to surface modifications, thanks to the presence of siloxane (≡Si-O-Si≡) and silanol (≡Si-OH) groups [25]. Silica has osteoinductive properties due to its interaction with calcium and phosphorus ions through silanol groups [26]. Nanostructures based on mesoporous silica, thanks to their active surface, have been used in implantology for the regeneration of bone tissues [26–29]. Perlite, on the other hand, is a natural, amorphous volcanic glass. It consists of sulfur oxide (SiO_2), aluminum oxide (Al_2O_3), potassium oxide (K_2O), sodium oxide (Na_2O), calcium oxide (CaO) and magnesium oxide (MgO) and water [30, 31]. This mineral is used as a nanofiller in the polymer matrix, which leads to better mechanical and physicochemical properties, such as greater mechanical strength, elastic modulus, and stiffness, as well as lower air permeability [30]. The advantages also include its high porosity, which significantly increases the specific surface area of the target composite. Perlite has high thermal properties and fire resistance, which is why it is considered a functional additive to a wide range of polymers and biopolymers in many industries [31, 32].

The aim of tissue engineering is to select appropriate materials with precisely defined chemical, physical and mechanical properties to restore, maintain or improve damaged tissues or entire organs. The interaction between biomaterials and surrounding tissues is a key issue when selecting appropriate components [33]. Currently, autografts and allografts are commonly used in implantology, but these procedures may be invasive and cause pain and infections at the site of bone tissue harvesting. Therefore, the use of synthetic grafts has been proposed as an alternative treatment. Due to their bioresorbability, nontoxicity, biodegradability and biocompatibility, polyurethanes (PUR) are suitable for applications in tissue engineering [15, 34]. These are synthetic elastomers whose physicochemical properties can be modified by changing the proportion of soft and hard segments [35]. The stability and morphology properties of PUR depend on the segregation of microphases between soft and hard segments. The presence of highly polar groups in rigid segments results in increased microphase separation, resulting in higher glass transition and melting temperatures. This leads to increased mechanical strength of the biomaterial [34]. Among synthetic polymers, polyurethane has become one of the most versatile materials that can be used, among others, as an orthopedic implant, coating for drainage devices and material for stabilizing bone fractures. The diversity of applications results from the fact that, thanks to chemical modification of their composition, polyurethanes can imitate many different structures of human tissues. Thanks to specific manipulation of the composition, polyurethanes imitate both the compact structure of cortical bone and the trabecular structure of cancellous bone [36]. Polyurethanes exhibit a much wider range of mechanical properties than other biomedical polymers. Moreover, polyurethanes can calcify, so this feature becomes advantageous for bone replacement [37–40].

Regenerative medicine is a dynamically developing field of science. There is a constant search for new material systems that will meet the criteria of materials dedicated to medicine, which is why cooperation between doctors and the academic community - scientists - is so important.

The aim of the work was to obtain bone-like materials ideal for making prototypes that could be used as teaching aids for medical students and in orthopedic treatment. Therefore, in this work, epoxy resin was selected as the matrix for creating artificial bone. Calcium carbonate ($CaCO_3$) and a mixture of silica (SiO_2) and perlite were used as fillers. The bone filling was polyurethane foam (PUR).

EXPERIMENTAL PART

Materials

DABCO 1,4-diazabicyclo[2.2.2]octane (Merck KGaA, Darmstadt, Germany), ABS filament, Spectrum Filaments (Pecice, Poland), ethylene glycol (Pol-Aura, Zawroty, Poland), silica (Aerosil MOX 80, OQEMA Ltd, Ozorkow, Poland), MDI 4,4'-diisocyanatediphenylmethane (Chem Distribution, Barendrecht, The Netherlands), perlite (ZGM Zebiec PLC, Starachowice, Poland), polyether polyol Rokopol M1170 (ethylene oxide and propylene oxide based on glycerin, PCC Rokita SA, Brzeg Dolny, Poland), silicone (ZA 22 MOULD, Zhermack, Badia Polesine, Italy), hardener (Z1, Sarzyna Chemical Ltd, Nowa Sarzyna, Poland), calcium carbonate ($CaCO_3$, Warchem Ltd, Zakręt, Poland), epoxy resin (Epidian 624, Sarzyna Chemical Ltd, Nowa Sarzyna, Poland) were used in this research.

Preparation of an artificial bone prototype

The artificial bone prototype was obtained in a three-step process. In the first stage, a design of two elements was prepared in the UP-Studio program - the external one (in the form of an empty cylinder) and the internal one (in the form of a filling rod) (Fig. 2). The elements were printed on a 3D printer (TierTime Up Box+, Beijing, China). Prototypes made of ABS filament were intended for further stages. The internal element of the mold is made of silicone so that it does not stick to the resin (Fig. 3a). For this purpose, the previously cut forms were connected to each other, leaving the outer element inside, and the center was filled with silicone (Fig. 3b). After the silicone hardened, a mold was prepared (Fig. 3c), in which an internal element made of silicone was placed, and then the mold was connected. In the next stage, composites

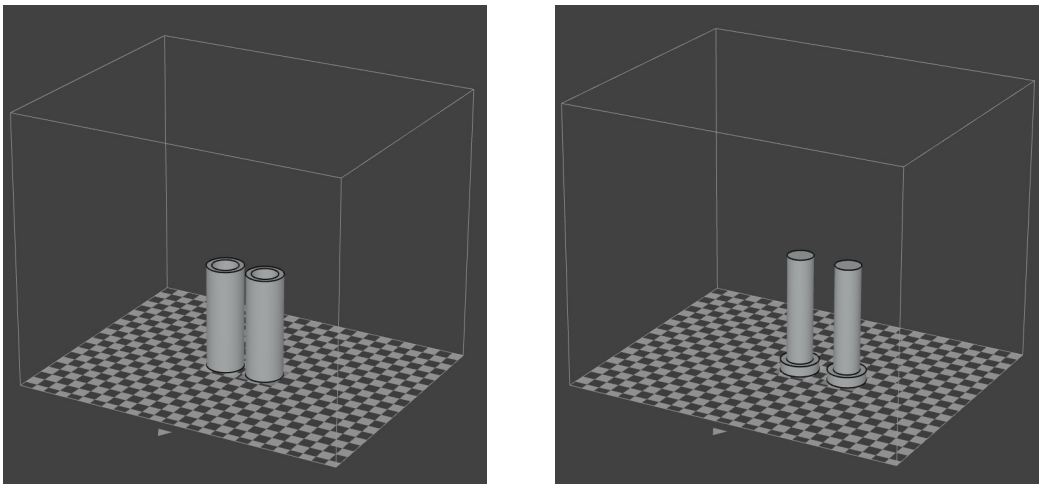

Fig. 2. Design of samples made in UP-Studio program

Fig. 3. Stages of obtaining a silicone mold: a) a model printed from ABS attached to the bottom of the cup, b) a cup with 3D model filled with silicone, c) a silicone mold with the model inside

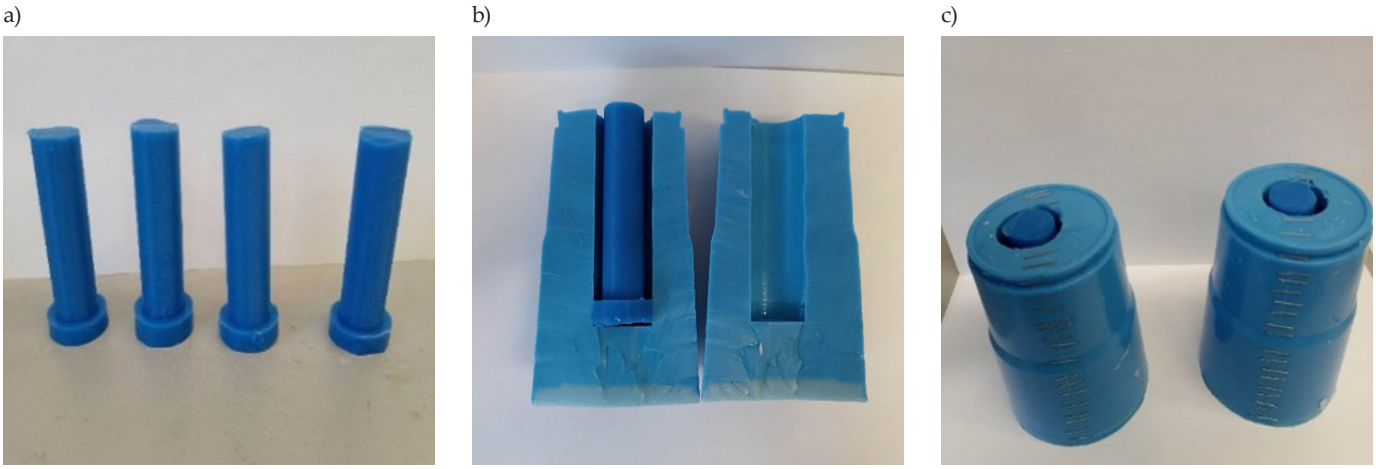

Fig. 4. Preparation of silicone molds and molding core: a) internal mold element, b) external and internal mold elements, c) finished mold

were prepared based on epoxy resin filled with calcium carbonate, perlite, and silica in appropriate proportions (Table 1). The process was carried out using a high-speed homogenizer (Dispermat, type D-51580, with a turbine mixer Getzmann Gmbh, Reichshof, Germany) for approximately 30 min at different speeds (500–2500 rpm). Then the hardener (12 wt%) was added. Finally, bone prototypes were obtained using silicone molds. In the third stage, the bone prototypes (cylinders) were filled with polyurethane foam, which was obtained by intensively mixing the ingredients (Table 2) until foaming began.

T a b l e 1. Composition of the composites

Sample	Filler	Content, wt%/wt%
Unfilled resin (UF)	–	–
M3	Perlite/silica	3/3
M5		5/5
M7		7/7
M50	Calcium carbonate	50
M60		60
M70		70

T a b l e 2. Composition of polyurethane foam

Components	Content, wt%
Polyol	29.9
MDI	64.4
Silicone	0.4
Water	1.7
Ethylene glycol	3.3
DABCO	0.8

Methods

Rockwell hardness was measured according to the PN-EN ISO 6508 standard using a Zwick/Roell hardness tester (Zwick GmbH & Co., Ulm, Germany) at ambient temperature. A load of 132 N was used for unfilled samples and 385 N for filled samples. Compressive properties were determined in accordance with the PN-EN ISO 604 standard at ambient temperature and a testing speed of 10 mm/min using an Instron 5967 testing machine (Instron, Grove City, PA, USA) and the Aramis system. This system is used to optically analyze strains, stresses, and displacements of materials in three dimensions. Compressive modulus was calculated at a testing speed of 5 mm/min (up to 1% tensile strain).

RESULTS AND DISCUSSION

Compressive properties

Figures 5 and 6 present a visualization of the displacements resulting from applying the maximum load to the sample placed vertically and horizontally in the apparatus, along three axes: X, Y and Z. Figure 5 illustrates the displacement of the unfilled sample. The maximum force applied to the vertically placed sample was 21.3 kN.

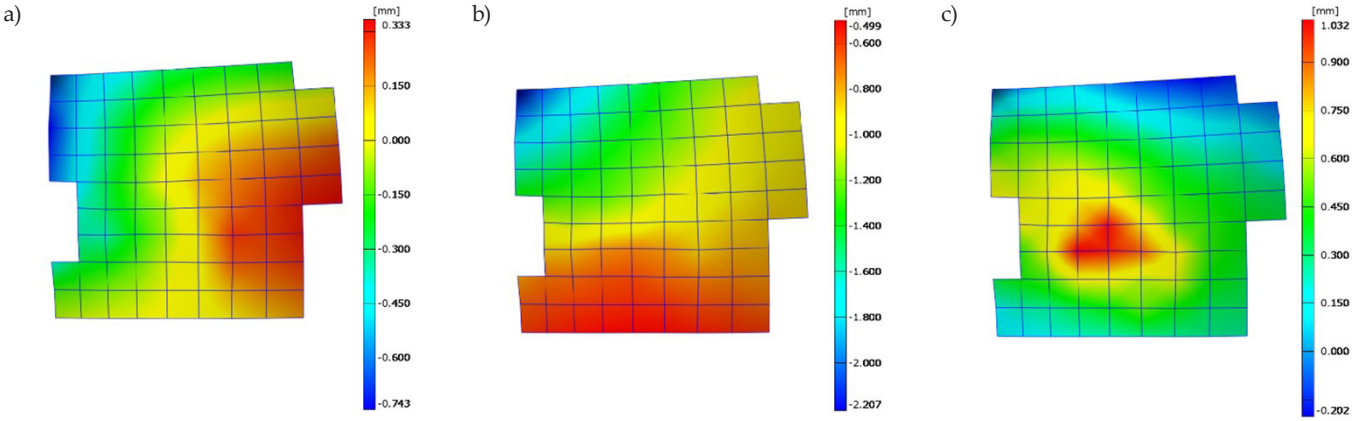

Fig. 5. Maps of displacement of the unfilled sample placed vertically: a) X axis, b) Y axis, c) Z axis

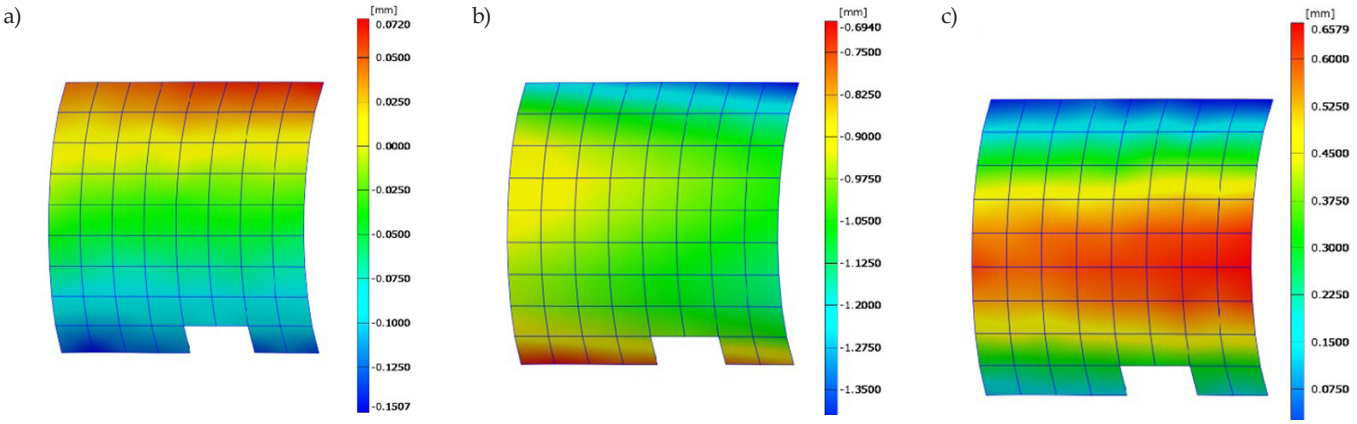

Fig. 6. Maps of displacement of the unfilled sample placed horizontally: a) X axis, b) Y axis, c) Z axis

T a b l e 3. Displacement of the composities

Sample	Displacement, %			
	Vertically		Horizontally	
	X	Y	X	Y
UF	7.50	1.34	0.33	1.63
M3	17.30	1.53	0.36	0.94
M5	4.06	2.28	0.21	0.89
M7	6.26	2.17	0.51	1.74
M50	10.00	2.00	0.08	0.65
M60	3.64	0.25	0.47	1.88
M70	2.38	0.39	0.25	0.96

The largest displacement of this sample in the X, Y and Z axes was recorded as 0.333 mm, -0.499 mm, and 1.032 mm, respectively.

Fig. 6 shows the distribution of displacement along the three axes of the UF sample placed horizontally in the apparatus. The resulting displacement under the influence of the maximum force of 1.7 kN reaches 0.072 mm for the X axis, -0.694 for the Y axis and 0.658 for the Z axis. The displacement along the Z axis allows us to conclude that there was a uniform shift in the central part of the samples. The smallest defects were observed in the X axis for the sample placed horizontally (Fig. 6a), where the largest displacement occurred at the point where the force was applied.

The results presented in Table 3 confirm that compressive strength of the samples increases with the increase in the amount of filler. Samples containing a hybrid filler consists of silica and perlite mixture are more brittle than those containing $CaCO_3$. As the amount of filler increases, the force needed to destroy the sample increases. The greatest damage was observed in the Z axis for vertically placed samples, and the smallest in the X axis for horizontally placed samples. EP filled with 70 wt.% $CaCO_3$ had the highest compressive strength, due to the lowest displacement.

The maximum load needed to destroy samples placed vertically in the apparatus increased with calcium carbonate content (Fig. 7a). The unfilled sample placed vertically was characterized by a lower load (about 20 kN) compared to samples filled with $CaCO_3$ and higher compared to samples filled with a hybrid filler (mixture of silica and perlite). An inverse correlation was observed in the case of the horizontally placed samples (Fig. 7b). The load needed to destroy the sample decreased as the $CaCO_3$ content increased. The opposite behavior was observed for a mixture of silica and perlite. In this case, the load needed to destroy the samples was much lower compared to samples filled with calcium carbonate. In the case of vertically placed samples, an increase in load was observed with increasing filler content, while for horizontally placed samples, the highest force was required to destroy the sample filled with silica and perlite (M5). It can be concluded that samples placed vertically withstand much greater loads than those placed horizontally.

Compressive stress

The compressive stress of samples placed vertically slightly increases with the filler content (Fig. 8a). However, the composites filled with $CaCO_3$ had much higher strength than that with the hybrid filler. Moreover, the compressive strength of the $CaCO_3$-filled composites is slightly higher than that of the UF sample. In the case of samples placed horizontally (Fig. 8b), the stresses were much lower, reach-

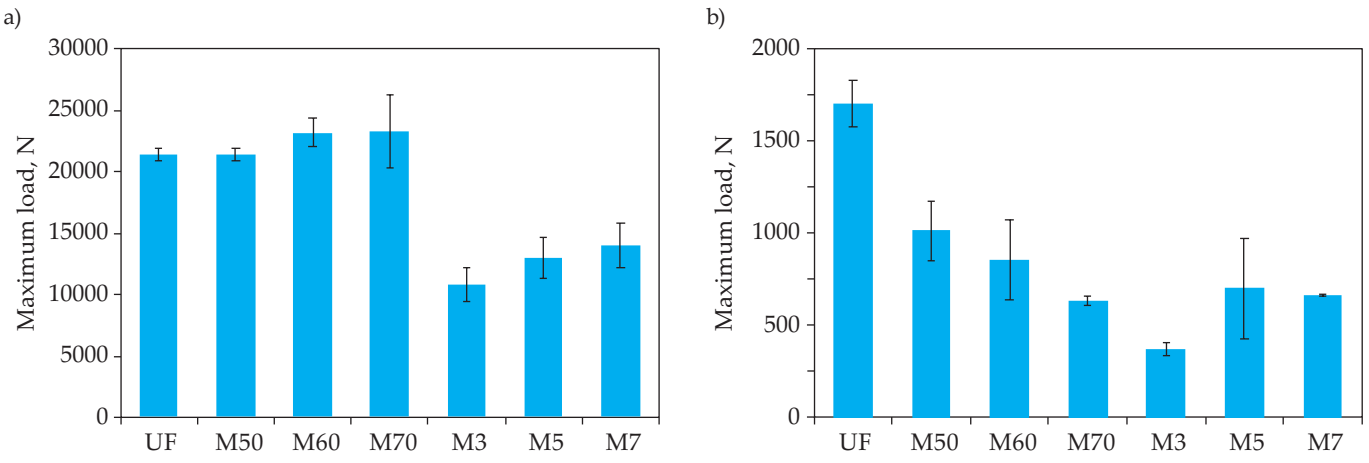

Fig. 7. Maximum load for samples placed: a) vertically, b) horizontally

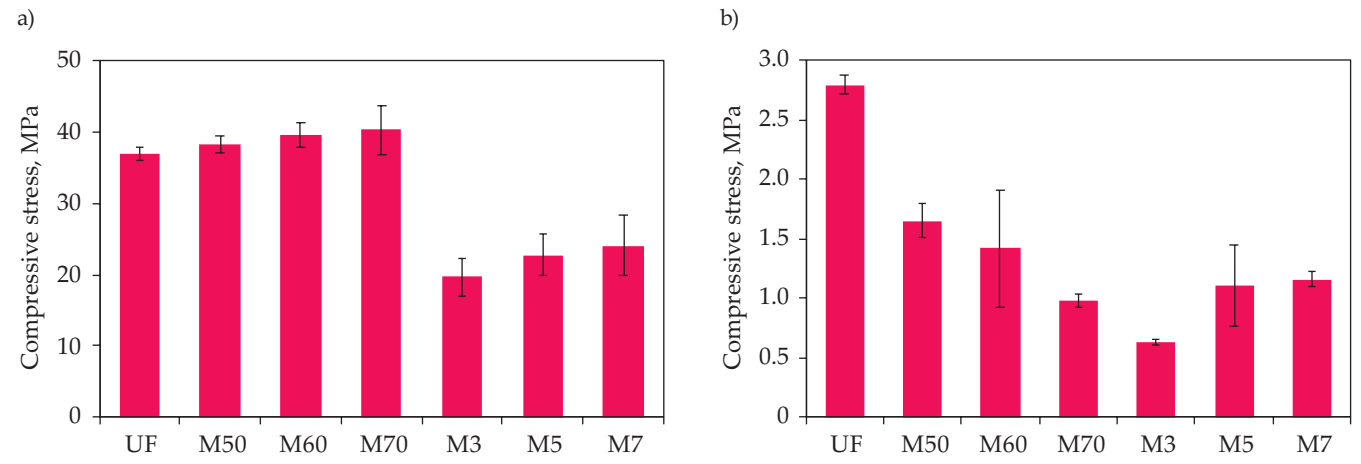

Fig. 8. Compressive stress for samples placed: a) vertically, b) horizontally

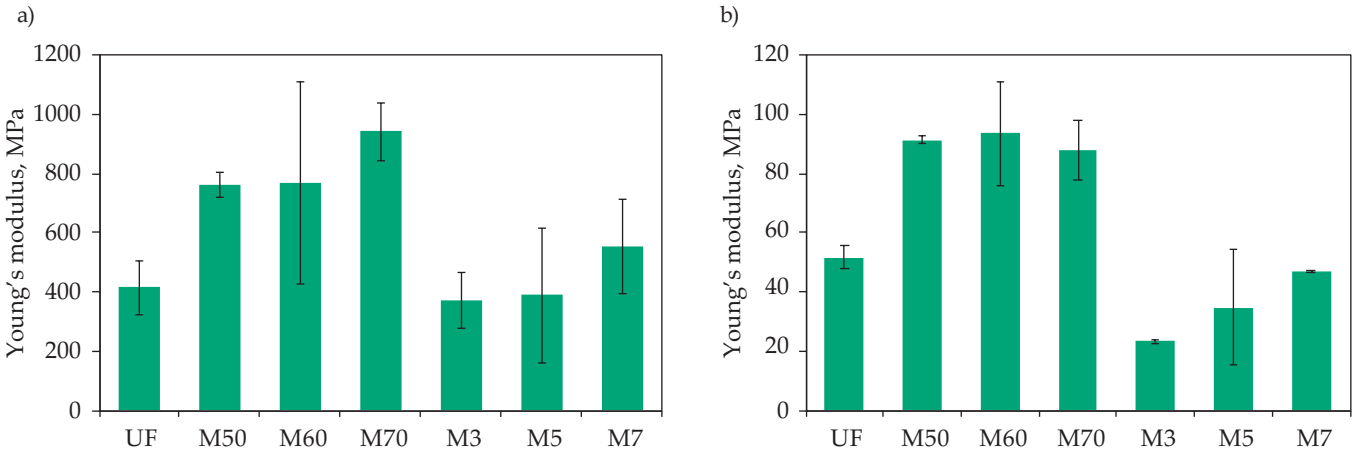

Fig. 9. Young's modulus for samples placed: a) vertically, b) horizontally

ing approximately 2.8 MPa for the unfilled sample and decreasing with increasing $CaCO_3$ content. The compressive stress undergoes a similar behavior as the maximum load (Fig. 7). Moreover, in the case of samples placed horizontally, the M3 sample achieved the lowest value of compressive stress among all the tested composites.

Young's modulus

The Young's modulus of a vertically placed, unfilled sample is about 400 MPa and increases with increasing calcium carbonate content to 900 MPa. Similar relationships were observed for horizontally placed samples, for which the modulus is about 50 MPa for the unfilled sample and approximately 85 MPa for the M70 sample. The obtained results indicate a lower tendency of composites to deform. In the case of the hybrid filler, an increase in modulus was observed for vertically placed samples. However, in the case of horizontally placed samples, the Young modulus is the highest for the unfilled sample and the lowest for the M3 sample. Consequently, the larger the module, the smaller the displacement. The largest modulus, and consequently, the smallest displacement and the highest compressive strength, were obtained for the composite containing 70% $CaCO_3$.

Rockwell hardness

Figure 10 shows that the Rockwell hardness increases as a function of the calcium carbonate content, which is a typical behavior for fillers [41]. Moreover, the addition of the hybrid filler causes a decrease in hardness, which, however, increases slightly as the filling increases. This may be due to the lower strength and stiffness of composites filled with a mixture of silica and perlite, resulting from a much lower filler content compared to calcium carbonate.

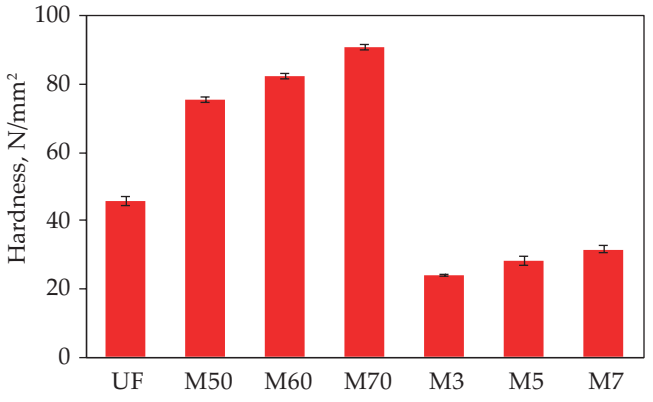

Fig. 10. Hardness of the composites

CONCLUSIONS

Composites based on epoxy resin with the addition of $CaCO_3$ and the hybrid filler consisting of silica and perlite mixture were developed to obtain artificial bone. The orientation of the sample (vertical or horizontal) has been shown to influence the compression properties. For vertically placed samples, it was found that the addition of calcium carbonate resulted in a significant increase in both maximum load and Young's modulus, unlike samples without filler. In the case of the hybrid filler, an inverse relationship was observed. The beneficial effect of $CaCO_3$ on compressive stress and Young's modulus is clearly visible. Moreover, the fillers resulted in a reduction in the maximum load compared to EP. Calcium carbonate significantly increased the hardness, which increased as a function of the filler content. However, the hybrid filler decreased hardness. The obtained anatomical bone model (M70) did not differ from natural bone in terms of structure and properties. Implants of this type can be used as teaching aids for medical students and in orthopedic treatment.

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Authors contribution

D.F. – formal analysis, investigation, writing-original draft; K.B. – methodology, formal analysis, investigation, writing-original draft, visualization. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare no conflict of interest.

REFERENCES

[1] Chalmin P.: "The history of plastics: from the Capitol to the Tarpeian Rock" in "Field Actions Science Reports, Special Issue 19", Institut Veolia, online 2019, p. 6. http://journals.openedition.org/factsreports/5071

[2] Szczygielska M.: *Kultura Współczesna* **2021**, *1(113)*, 28. https://doi.org/10.26112/kw.2021.113.03

[3] Żuchowska D.: „Polimery konstrukcyjne. Wprowadzenie do technologii i stosowania", Wydawnictwa Naukowo-Techniczne, Warszawa 1995. p. 19, 161.

[4] Wortmann M., Frese N., Brikmann J. *et al.*: *Macromolecular Symposia* **2021**, *395(1)*, 2000242. https://doi.org/10.1002/masy.202000242

[5] Valerga Puerta A.P., Moreno Sanchez D., Batista M. *et al.*: *Journal of Manufacturing Processes* **2018**, *35*, 721. https://doi.org/10.1016/j.jmapro.2018.08.033

[6] Oleksy M., Budzik G., Kozik B., Gardzińska A.: *Polimery* **2017**, *62(1)*, 3. https://doi.org/10.14314/polimery.2017.003

[7] Ozdil D., Aydin H.M.: *Journal of Chemical Technology and Biotechnology* **2014**, *89(12)*, 1793. https://doi.org/10.1002/jctb.4505

[8] Culmone C., Smit G., Breedveld P.: *Additive Manufacturing* **2019**, *27*, 461. https://doi.org/10.1016/j.addma.2019.03.015

[9] Puppi D., Chiellini F.: *Applied Materials Today* **2020**, *20*, 100700. https://doi.org/10.1016/j.apmt.2020.100700

[10] Pietrzak W.S., Sarver D., Verstynen M.: *Bone* **1996**, *19(1)*, S109. https://doi.org/10.1016/S8756-3282(96)00139-1

[11] Gadomska-Gajadhur A., Łojek K., Szymaniak M. et al.: Inżynieria Tkankowa 2018, 51. https://www.researchgate.net/profile/Agnieszka-Gadomska-Gajadhur/publication/327141603_Materialy_porowate_do_regeneracji_tkanki_chrzestnej_i_kostnej/links/5b9f8e0745851574f7d1cbb1/Materialy-porowate-do-regeneracji-tkanki-chrzestnej-i-kostnej.pdf

[12] Mustafa N.N.M, Kadir A.Z.A., Ngadiman N.H.A. *et al.*: *Journal of Mechanical Engineering and Sciences* **2019**, *14(1)*, 6417. https://doi.org/10.15282/jmes.14.1.2020.17.0502

[13] Ahmad M.N., Alkahari M.R., Basir M.F.M. *et al.*: "Optimization of vacuum casting process parameters using Taguchi method" in "Proceedings of Mechanical Engineering Research Day", Centre of Advanced Research of Energy, Melaka 2018. p. 146.

[14] Kuo C.-C., Li D.-Y., Lin Z.-C. *et al.*: *Polymers* **2021**, *13(23)*, 4126. https://doi.org/10.3390/polym13234126

[15] Marzec M., Kucińska-Lipka J., Kalaszczyńska I. *et al.*: *Materials Science and Engineering: C* **2017**, *80*, 736. https://doi.org/10.1016/j.msec.2017.07.047

[16] Bartmański M.: „Wytwarzanie powłok hydroksyapatytowych z osłoną biologiczną na stopie tytanu". Rozprawa doktorska, Gdańsk 2019. https://mostwiedzy.pl/en/publication/wytwarzanie-powlok-hydroksyapatytowych-z-oslona-biologiczna-na-stopie-tytanu,156526-1

[17] Makrenek M., Belka R., Żórawski W. *et al.*: *Medycyna Pracy* **2018**, *69(6)*, 651. https://doi.org/10.13075/mp.5893.00725

[18] A. Bukowska, Prof. PRz, (2022). *Biomateriały*, Wykład, Politechnika Rzeszowska, Rzeszów
[19] Jeong J., Kim J.H., Shim J.H. *et al.*: *Biomaterials Research 2019,* 23(1), article ID s40824-018-0149-3. https://doi.org/10.1186/s40824-018-0149-3
[20] Oudadesse H., Derrien A.C., Lucas-Girot A. *et al.*: *Instrumentation Science and Technology* **2004**, *32(5)*, 545. https://doi.org/10.1081/CI-200029803
[21] Kim S., Park C.B.: *Biomaterials* **2010**, *31(25)*, 6628. https://doi.org/10.1016/j.biomaterials.2010.05.004
[22] Huang Y., Cao L., Parakhonskiy B.V. *et al.*: *Pharmaceutics* **2022**, *14(5)*, 909. https://doi.org/10.3390/pharmaceutics14050909
[23] Krajewska B., Raczak K.: *Ochrona Środowiska* **2019**, *41(1)*, 31.
[24] Szeleszczuk Ł.J.: „Spektroskopowe badania skorupy jaja kurzego". Rozprawka doktorska, Wydział Farmaceutyczny Warszawski Uniwersytet Medyczny, Warszawa 2015
[25] Kurczewska J.: *Wiadomości Chemiczne* **2022**, *76*(*7–8*), 529. https://doi.org/10.53584/wiadchem.2022.7.3
[26] Jeon H., Yun S., Choi E. *et al.*: *Journal of Industrial and Engineering Chemistry* **2019**, *79*, 41. https://doi.org/10.1016/j.jiec.2019.04.050
[27] Al-Harbi N., Mohammed H., Al-Hadeethi Y. *et al.*: *Pharmaceuticals* **2021**, *14(2)*, 75. https://doi.org/10.3390/ph14020075
[28] Ghosh S., Webster T.J.: *Frontiers in Materials* **2021**, *8*, 692309. https://doi.org/10.3389/fmats.2021.692309
[29] Arcos D., Vallet-Regí M.: *Acta Biomaterialia* **2010**, *6(8)*, 2874. https://doi.org/10.1016/j.actbio.2010.02.012
[30] Lapčík L., Vašina M., Lapčíková B. *et al.*: *Nanotechnology Reviews* **2020**, *9(1)*, 1491. https://doi.org/10.1515/ntrev-2020-0113
[31] Aval S.T., Davachi S.M., Sahraeian R. *et al.*: *Polymer Testing* **2020**, *91*, 106779. https://doi.org/10.1016/j.polymertesting.2020.106779
[32] Zhang H., Dong Q., Lu J. *et al.*: *Journal of Energy Storage* **2023**, *65*, 107374. https://doi.org/10.1016/j.est.2023.107374
[33] Bil M., Ryszkowska J., Woźniak P. *et al.*: *Acta Biomaterialia* **2010**, *6(7)*, 2501. https://doi.org/10.1016/j.actbio.2009.08.037
[34] Szczepańczyk P., Szlachta M., Złocista-Szewczyk N. *et al.*: *Polymers* **2021**, *13(6)*, 946. https://doi.org/10.3390/polym13060946
[35] Dulinska-Molak I., Jaroszewicz J., Kurzydlowski K.J.: *Journal of Bioprocessing and Biotechniques* **2014**, *4(3)*, 1000153. https://doi.org/10.4172/2155-9821.1000153
[36] Filip N., Radu I., Veliceasa B. *et al.*: *Coatings* **2022**, *12(10)*, 1544. https://doi.org/10.3390/coatings12101544
[37] Meskinfam M., Bertoldi S., Albanese N. *et al.*: *Materials Science and Engineering: C* **2018**, *82*, 130. https://doi.org/10.1016/j.msec.2017.08.064
[38] Horak Z., Dvorak K., Zarybnicka L. *et al.*: *Materials* **2020**, *13(20)*, 4560. https://doi.org/10.3390/ma13204560
[39] Vinay V.C., Varma D.M., Chandan M.R. *et al.*: *Polymer Bulletin* **2022**, *79*, 4233. https://doi.org/10.1007/s00289-021-03705-x
[40] Boissard C.I.R., Bourban P.E., Tami A.E. *et al.*: *Acta Biomaterialia* **2009**, *5(9)*, 3316. https://doi.org/10.1016/j.actbio.2009.05.001
[41] Mostoufi A., Bavarsad N., Aryanfar S. *et al.*: *Pharmaceutical Sciences* **2018**, *24*, 227. https://doi.org/10.15171/ps.2018.33

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