NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ
Faculty of Chemistry

Department of Biomedical Chemistry and Polymers

Dr Marta Ziegler-Borowska

Summary of Professional Accomplishments

Field of science: natural sciences

Scientific discipline: chemical sciences

Torun 2022

1. Name

Marta Ziegler-Borowska
(Family name: Ziegler)

2. Diplomas, degrees conferred in specific areas of science or arts, including the name of the institution which conferred the degree, year of degree conferment, the title of the PhD dissertation

- **2009 PhD degree in Chemistry** (2 December 2009)

  Nicolaus Copernicus University in Toruń,
  Department of Organic Chemistry
  Doctoral dissertation title:
  "Synthesis of 4-dihydroxyborylphenylalanine analogues".
  Supervisor: Prof. Dr. Marek Zaidlewicz
  Reviewers: Prof. Dr.-Ing. Janusz Serwatowski
  Prof. Dr. Zbigniew Leśnikowski

- **2002 Master of Science in Chemistry**

  Nicolaus Copernicus University in Toruń,
  Department of Organic Chemistry
  Thesis title:
  "*Synthesis of a-methyl-p-dihydroxyborylphenylalanine*".
  Promoter: Dr Adam Dzielendziak
  Reviewer: Prof. Dr. Marek Zaidlewicz

- **2000 Bachelor of Chemistry**

  Nicolaus Copernicus University in Toruń,
  Department of Organic Chemistry
  Bachelor thesis title:
  "Synthesis and use of benzene, toluene and xylenes".
  Supervisor: Prof. Dr. Marek Zaidlewicz
  Reviewer: Prof. Dr. Halina Kaczmarek

3. Information on employment in research institutes or faculties/departments or school of arts

- **2012- currently Assistant Professor**

  Department of Biomedical Chemistry and Polymers (Former name Department of Chemistry and Photochemistry of Polymers), Faculty of Chemistry, Nicolaus Copernicus University in Toruń, Torun

- **01.02. 2010 - 2012 Assistant**

  Department of Chemistry and Photochemistry of Polymers, Faculty of Chemistry, Nicolaus Copernicus University in Toruń, Torun

- **15.02.2006 - 2010 Assistant**

  Department of Organic Chemistry, Faculty of Pharmacy, Medical College im. L. Rydygier in Bydgoszcz, Nicolaus Copernicus University in Toruń, Bydgoszcz

4 Description of the achievements, set out in art. 219 para 1 point 2 of the Act).

(a) Title of scientific achievement

Polysaccharide functionalized magnetic nanoparticles - synthesis, characterization, and biomedical applications

The basis for the application for a habilitation is a series of, thematically coherent and related, nine original scientific articles (eight co-authored papers, one independent paper) published between 2014 and 2020 in scientific journals (Q1-Q2) having an IF (from the year of publication) ranging from 1.781 to 6.707 (according to. JCR) with a total number of citations (excluding self-citations) of 183. In six papers I am the first and corresponding author; in two first author, and in one corresponding author. Four articles were written as part of the NCN Sonata 8 grant under my direction**,** 2014/15/D/NZ7/01805; *Synthesis and study of the interaction of magnetic nanoparticles coated with human serum protein with selected drugs under normal and artificially induced oxidative stress conditions* (2015-2019)**.**

The publications included in the achievement form a monothematic series of works concerning the design and synthesis of new magnetic nanoparticles with a modified polysaccharide coating, their characterisation as well as biomedical applications.

(b) Publications included in the scientific achievement:

H1. Marta Ziegler-Borowska*, Tomasz Siódmiak, Dorota Chełminiak, Aleksandra Cyganiuk, Michał P Marszałł. Magnetic nanoparticles with surfaces modified with chitosan-poly [N-benzyl-2-(methacryloxy)-N, N-dimethylethanaminium bromide] for lipase immobilization, *Appl. Surf. Sci.,* **2014,** *288*, 641-648; doi: 10.1016/j.apsusc.2013.10.088

IF_{2014} 2,711 ; IF_{2021} 7,392; MNiSW points 140, Q1

14 citations without self-citation

My contribution to the publication consisted of planning and supervising the research, designing the structure of the PQ polymer and the magnetic nanoparticles

coated with it, developing the method of synthesis and interpreting the results of the analyses and characterisation of the material, and writing the entire manuscript on the synthesis and characterisation of the magnetic nanoparticles, as well as the entire response to the reviews.

H2. Marta Ziegler-Borowska*, Dorota Chełminiak, Tomasz Siódmiak, Adam Sikora, Michał Piotr Marszałł, Halina Kaczmarek, Synthesis of new chitosan coated magnetic nanoparticles with surface modified with long-distanced amino groups as a support for bioligands binding. *Mat. Lett*., **2014**, *132*, 63-65; doi: 10.1016/j.matlet.2014.06.020

IF$_{2015}$ 2,489 ; IF$_{2021}$ 3,574 ; MNiSW points 70, Q2

14 citations without self-citation

My contribution to the publication consisted of planning and supervising the research, designing the structure of the modified chitosan coating the nanoparticles, developing the method and optimising its synthesis and coating the magnetic nanoparticles with it, optimising the synthesis of the nanoparticles as well as interpreting the analyses and characterising the material obtained, writing, editing the entire manuscript and responding to reviews.

H3. Marta Ziegler-Borowska, Dorota Chełminiak, Halina Kaczmarek*, Thermal stability of magnetic nanoparticles coated by blends of modified chitosan and poly (quaternary ammonium) salt. *J. Therm. Anal. Calorim*., **2015**, *119*, 499-506; doi: 10.1007/s10973-014-4122-7

IF$_{2015}$ 1,781 ; IF$_{2021}$ 4,755 ; MNiSW points 70, Q1

61 citations without self-citation

My contribution to the publication consisted of planning the research, designing the structure of the polymer coating covering the nanoparticles, planning, selecting the optimal conditions and carrying out their synthesis, characterisation of the material as well as writing the manuscript and responding to reviews.

H4. Marta Ziegler-Borowska, Dorota Chełminiak, Halina Kaczmarek*, Anna Kaczmarek-Kędziera, Effect of side substituents on thermal stability of the modified chitosan and its nanocomposites with magnetite. *J. Therm. Anal. Calorim*.,**2016**, 124, 1267-1280; doi: 10.1007/s10973-016-5260-x

IF$_{2016}$ 1,953 ; IF$_{2021}$ 4,755 ; MNiSW points 70, Q1

40 citations without self-citation

My contribution to the publication consisted in the conception of the research, design of the structure of the modified chitosan materials (CS-1,CS-2 and CS-3), planning and optimising the conditions and carrying out their synthesis and characterisation of the material. I planned, carried out and optimised the conditions

for the synthesis of magnetic nanoparticles coated with modified chitosan materials, wrote the manuscript and responded to the reviews.

H5. Marta Ziegler-Borowska*, Dorota Chelminiak-Dudkiewicz, Tomasz Siódmiak, Adam Sikora, Katarzyna Wegrzynowska-Drzymalska, Joanna Skopinska-Wisniewska, Halina Kaczmarek, Michał P. Marszałł, Chitosan-Collagen Coated Magnetic Nanoparticles for Lipase Immobilization-New Type of "Enzyme Friendly" Polymer Shell Crosslinking with Squaric Acid. *Catalysts*, **2017,** *7*, 26; doi: 10.3390/catal7010026
IF$_{2017}$ 3,465 ; IF$_{2021}$ 4,501 ; MNiSW points 100, Q2
30 citations without self-citation

My contribution to the publication included planning and supervising all the research carried out under my NCN Sonata 8 grant; designing the composition of the polymer coatings covering the magnetic nanoparticles, designing the use of square acid as a cross-linking agent for collagen and chitosan, planning, optimising the and execution of the synthesis of the nanoparticles, characterisation of the nanoparticles, writing, editing the entire manuscript and responding to reviews.

H6. Marta Ziegler-Borowska*, Magnetic nanoparticles coated with aminated starch for HSA immobilization-simple and fast polymer surface functionalization. *Int. J. Biol. Macromol.*, **2019**, *136*,106-114 ; doi: 10.1016/j.ijbiomac.2019.06.044
IF$_{2019}$ 5.162 ; IF$_{2021}$ 8.025 ; MNiSW points 100, Q1
8 citations without self-citation

H7. Marta Ziegler-Borowska*, Kinga Mylkie, Mariana Kozlowska, Pawel Nowak, Dorota Chelminiak-Dudkiewicz, Anna Kozakiewicz, Anna Ilnicka, Anna Kaczmarek-Kedziera, Effect of Geometrical Structure, Drying, and Synthetic Method on Aminated Chitosan-Coated Magnetic Nanoparticles Utility for HSA Effective Immobilization. *Molecules*, **2019**, *24*, 1925; doi: 10.3390/molecules24101925
IF$_{2019}$ 3,267 ; IF$_{2021}$ 4,927; MNiSW points 140, Q2
3 citations without self-citation

My contribution to the publication consisted of planning and supervising all the research carried out under my NCN Sonata 8 grant, designing the magnetic nanoparticles, their synthesis and drying methods, planning the HSA immobilisation methods, characterising and interpreting the results and writing, editing the entire manuscript and responding to reviews.

H8. Marta Ziegler-Borowska*, Kinga Mylkie, Pawel Nowak, Patryk Rybczynski, Adam Sikora, Dorota Chelminiak-Dudkiewicz, Anna Kaczmarek-Kedziera, Testing for Ketoprofen Binding to HSA Coated Magnetic Nanoparticles under Normal

Conditions and after Oxidative Stress. *Molecules*, **2020**, *25*, 1945; doi: 10.3390/molecules25081945
IF_{2020} 4.412, IF_{2021} 4.927; MNiSW points 140, Q2
3 citations without self-citation

My contribution to the publication consisted of planning and supervising all the research carried out under the NCN Sonata 8 grant that I managed, developing and optimising the HSA immobilisation method, planning and optimising the HSA free-drug and HSA immobilised-drug interaction studies, interpreting the results obtained and writing, editing the entire manuscript and responding to the reviews.

H9. Dorota Chelminiak-Dudkiewicz, Patryk Rybczynski, Aleksander Smolarkiewicz-Wyczachowski, Dariusz T Mlynarczyk, Katarzyna Wegrzynowska-Drzymalska, Anna Ilnicka, Tomasz Goslinski, Michał P Marszałł, **Marta Ziegler-Borowska*** , Photosensitizing potential of tailored magnetite hybrid nanoparticles functionalized with levan and zinc(II) phthalocyanine. *Appl. Surf. Sci.*, **2020**, *524*,146602; doi:10.1016/j.apsusc.2020.146602
IF_{2020} 6.707; IF_{2021} 7.392; MNiSW points 140, Q1
10 citations without self-citation

My contribution to the publication consisted of planning and supervising the research, designing the structure of the nanoparticles, optimising the conditions for the synthesis of the photosensitised magnetic nanoparticles, interpreting the results and writing and editing the manuscript as well as discussing with reviewers and responding to reviews.
* Corresponding author

Table 1. Summary of impact factor (IF) and MNiSW scores for papers **H1-H9** included in the scientific achievement

Summary IF impact factor (according to JCR list)	**50,248**
Average IF value (according to JCR list)	**5,583**
Summative score of the MNiSW	**970**
Average number of MNiSW points	**108**
Total number of citations excluding self-citations (According to Scopus.)	**183**

The research described in papers **H1, H2, H5, H8** and **H9** was developed as part of a long-term collaboration with the Department of Medicinal Chemistry, Faculty of Pharmacy, UMK. In addition, paper **H9** is also the result of collaboration

with the Department of Chemical Technology of Medicinal Products of the University of Medical Sciences. K. Marcinkowski Medical University in Poznań.

The research described in publication **H7** includes results obtained as part of a collaboration with the Institute of Nanotechnology in Karlsruhe, Germany.

The four papers **H5-H8** are the result of research carried out under my SONATA 8 grant entitled "Synthesis and study of the interaction of magnetic nanoparticles coated with human blood serum proteins under normal and artificially induced oxidative stress", funded by the National Science Centre. "*Synthesis and study of the interaction of magnetic nanoparticles coated with human blood serum protein with selected drugs under normal and artificially induced oxidative stress"* funded by the National Science Centre (2014/15/D/NZ7/01805, 2015-2019).

- A description of my substantive contribution to each paper can be found in in Appendix 4 (section I.B) and above.
- Copies of papers H1-H9 identified as a scientific achievement are included in Appendix 5**.**
- Co-authors' statements outlining their substantive contributions to the individual papers can be found in Appendix 6.

(c) A detailed discussion of the scientific objective of the above work and the results achieved, together with a discussion of their possible use

Introduction

The development of nanotechnology has resulted in several developments that have recently translated into applications of nanostructures in many areas of science - particularly in the chemical and biomedical sciences [1-3]. Nanotechnology has significantly influenced the expansion of existing applications but has also allowed new phenomena and properties to be observed, opening the way for the design and synthesis of new materials. A particular group of nanomaterials are magnetic nanoparticles based on metals such as iron, cobalt, and nickel. The growing interest in obtaining these metals and their oxides at the nanometric scale is justified by the fact that at the 'nano' scale they exhibit properties that differ from classical materials. Firstly, they can be synthesised quite easily while controlling the size and significant homogeneity of the nanoparticles obtained. Secondly, they are characterised by superparamagnetism, which allows their position and displacement to be controlled by an external magnetic field. Furthermore, due to the superparamagnetism, magnetic nanoparticles enhance contrast in magnetic resonance imaging. All these features have made them very attractive materials for further basic and applied research. However, due to their susceptibility to oxidation and high toxicity, the use of pure metal nanoparticles in biomedical science is limited. Therefore, magnetic nanoparticles based on oxides of these elements are of greater interest in this area [4-8].

Iron oxides, due to their biocompatibility and relatively high chemical and colloidal stability, have become some of the most widely used materials to form the magnetic core of nanoparticles for biomedical science applications. The use of iron oxide-based magnetic nanoparticles in areas such as drug delivery, hyperthermia, tissue engineering, bioseparation, medical analytics or catalysis continues to grow, while at the same time, newer and newer materials are being sought that are designed for already specific application uses [9-16].

Covering the magnetic core with a coating composed of inorganic compounds, small-molecule organic compounds or polymers allows, on the one hand, to improve the stability of nanoparticles, to prevent their agglomeration, but, above all, to functionalise the surface of the material and control the properties of nanoparticles [17-21]. Appropriately designed magnetic nanoparticles can be the starting material for further modifications towards complex systems based on nanostructures.

The use of polymers to stabilise the magnetic core offers a number of possibilities especially in the area of application of the resulting nanomaterials.

Polymer-coated magnetic nanoparticles are usually characterised by greater homogeneity and stability than those coated with small-molecule compounds, as well as well-defined shape and surface properties, which can be designed according to the final use of the nanomaterial.

I became interested in the topic of magnetic nanoparticles at the end of 2010 while searching for new opportunities to combine my biomedical interests and synthetic skills with the topics pursued in the then Department of Chemistry and Photochemistry of Polymers, where I was hired in January 2010. As my research interests have always been directed towards the synthesis of materials for biomedical applications, I decided to choose iron oxide as the core for nanoparticles. Among the different types of iron oxide-based nanoparticles, the three most common structures are magnetite (Fe_3O_4), maghemite (Fe_2O_3) and mixed ferrites (MFe_2O_4 where M = Cobalt (Co), Manganese (Mn), Nickel (Ni) or Zinc (Zn)). Materials containing cobalt and nickel are, as I have already mentioned, toxic materials, which is why I did not consider them from the start. When obtaining materials for biomedical applications based on magnetite and maghemite, it is important to bear in mind that, especially on the nanometric scale, these oxides are susceptible to oxidation (magnetite oxidises to maghemite) and can generate reactive oxygen species that cause oxidative stress in the body, which can ultimately lead to cell damage through lipid peroxidation or damage to protein structures. These are reactions that are usually unfavourable for biomedical applications but can sometimes be desirable, as I will discuss in more detail when discussing the results in article **H9**. However, these reactions can be inhibited by using a coating to stabilise the superparamagnetic core of the nanoparticles [22-25].

Scientific objective and scope of work

At the time I decided to address the topic of magnetic nanoparticles, most of those described in the literature were constructed from a core stabilised by inorganic compounds (hybrids with SiO_2), small-molecule organic compounds such as citric acid or synthetic polymers [26-28]. Such coatings for the magnetic core, despite their many advantages, are unattractive from the point of view of subsequent biomedical applications, in particular if one considers the use of the nanomaterial inside the body, e.g. as a drug carrier.

As I mentioned in the introduction, polymeric materials seem to be particularly effective in stabilising the magnetic core, but as I had been aiming at the biomedical application of the nanoparticles I obtained, it was natural that I decided to focus on the synthesis of materials stabilised by biopolymers, of which polysaccharides seemed to be the most useful. In March 2012, at a promotion seminar, in the presence of Department staff, invited guests and the then Dean for Science, Prof. Andrzej Wojtczak, I presented in detail my **research plans related to** my **habilitation activity, concerning the design and synthesis of new magnetic nanoparticles based on a magnetite core with a modified polysaccharide coating**.

I decided to use magnetite as the core, due to the fact that maghemite can be transformed into insoluble and non-magnetic iron(III) hydroxide, which would be unfavourable. **As starting polysaccharides, I chose chitosan, starch and levan** due to their documented use in biomedical sciences and, above all, their relatively good solubility allowing the formation of a layer covering the magnetic core [29-34]. I planned to use the resulting nanoparticles as **carriers for bioligands such as blood serum proteins and drugs.** The purpose of depositing a drug or serum protein on the surface of magnetic nanoparticles was, as intended: to facilitate the handling of the protein material (easy separation from the supernatant after application of the magnet) and to obtain carrier-protein and carrier-drug systems that could and carrier-drug systems, which could find application in anticancer therapy using the superparamagnetic properties of the magnetite core [35].

The objective of the research presented in the series of publications **H1-H9** forms the basis of the scientific achievement and concerns the **surface design and synthesis of new, functional magnetic nanoparticles** coated with polysaccharides, modified polysaccharides, as well as their mixtures with other polymeric materials, **and then depositing human serum albumin (HSA) or a drug on such an optimised surface while retaining ligand activity.** An important element is the **ability to control the properties of the nanoparticles** by choosing the polysaccharide covering the core and modifying it accordingly, as well as selecting the conditions for the synthesis and drying conditions of the material. An important part of the research conducted and described here was also the **development of a new solvent-free method for the amination of aldehyde polysaccharides** [**H6-H7**], as well as the **use of HSA bound on the surface of nanoparticles to study its interaction with the drug under normal and artificially induced oxidative stress conditions** [**H8**], providing new opportunities in pharmaceutical analysis. The results described in publication **H9,** which concludes the postdoctoral thesis series, also indicate the ability of the magnetite core to generate singlet oxygen, which may show positive effects when combined with a suitable drug. Furthermore, this publication signals the direction of my current and future research.
I pursued my objective through the following research tasks:

- synthesis of chitosan-coated magnetic nanoparticles using various polysaccharide-coated cross-linking agents, such as glutaraldehyde, epichlorohydrin, and squaric acid [**H5**, **H8**].
- synthesis of a new polymer with amphiphilic properties and its use in a mixture with polysaccharides to stabilise the magnetite core of nanoparticles [**H1**, **H3**].
- The synthesis of aminated chitosan containing different numbers of amino groups per glucosamine unit, followed by the synthesis of magnetic nanoparticles coated with these polymers [**H2-H4**].

- synthesis of aminated starch and coated magnetic nanoparticles by a rapid and solvent-free amination reaction [**H6**] and application of this method to the synthesis of nanoparticles coated with aminated chitosan [**H7,H8**].
- Synthesis of levane-coated magnetic nanoparticles and deposition of a drug clinically used in photodynamic therapy on their surface [**H9**].
- Immobilisation on the surface of magnetic nanoparticles of human serum albumin [**H2, H6-H8**] and the use of HSA deposited on magnetic support to study the interaction with ketoprofen under normal and artificially induced oxidative stress conditions [**H8**].
- Evaluation of the effect of the polysaccharide coating covering the core of magnetic nanoparticles on the ability to control their properties and ligand-binding capacity [**H7, H8**].

While conducting my work related to my postdoctoral topics, I was awarded an NSC grant in the Sonata 8 competition for research included in the presented Achievement entitled *Synthesis and study of the interaction of magnetic nanoparticles coated with human serum protein with selected drugs under normal and artificially induced oxidative stress conditions*, (**2014/15/D/NZ7/01805)**.

Discussion of the results

1. Magnetic nanoparticles coated with polysaccharides

Polysaccharides are, along with proteins, nucleic acids, and lipids, one of the of the major classes of biomolecules. Due to their well-defined chemical structure, biocompatibility, and biodegradability, as well as sufficient hydrophilicity for biomedical applications, polysaccharides have been widely used successfully as materials in these applications [36-39]. Furthermore, polysaccharides are readily available and relatively inexpensive, which is important for the potential implementation of the results. Due to all the advantages mentioned above, I decided to choose polysaccharides as starting biopolymers to stabilise the magnetite core of the nanoparticles I obtained.

1.1 Nanoparticles coated with chitosan (CS) and its mixture with a cationic polymer (PQ)

Chitosan (CS) is a linear polysaccharide obtained by deacetylation of chitin. It is composed of randomly linked units of *N-acetylated* and deacetylated glucosamine units (**Fig.1**). The degree of deacetylation of chitosan determines its properties and hydrophilic-hydrophobic character. It is one of the most widely used polysaccharides in biomedical sciences due to its biocompatibility, low toxicity and immunostimulatory effects [40-42]. Due to the presence of primary amine groups

in the deacetylated units, chitosan is the only natural cationic polymer and has many commercial applications. When used as a material in biomedicine, it accelerates wound healing, has antimicrobial [43-46], antifungal [47-49], anticancer [50,51] and haemostatic [52-54] effects. The presence of reactive amino groups, in addition to the formation of ammonium ions in acidic media, also allows easy covalent and ionic cross-linking of this biopolymer, as well as chemical modifications of its structure, which proved to be crucial in my further studies.

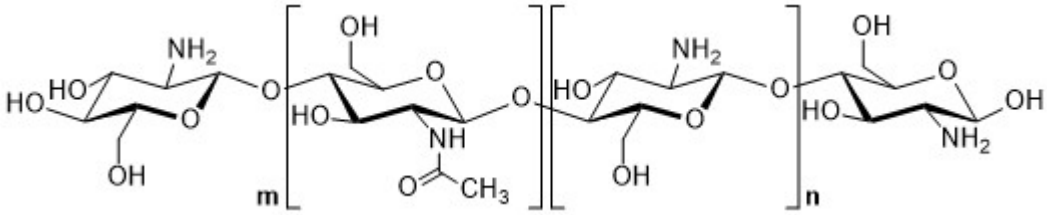

Fig.1. Structure of chitosan

In the first step, I obtained magnetite nanoparticles coated with a chitosan coating cross-linked with epichlorohydrin (**Fe_3O_4 -CS/Epi**), which, along with glutaraldehyde, is one of the most used chitosan cross-linking agents [55, 56]. Epichlorohydrin reacts with the hydroxyl groups of chitosan leaving, in contrast to glutaraldehyde, the amino groups free [57]. The method of nanoparticle synthesis I chose was the co-precipitation reaction [58,59]. This approach, due to the solubility of chitosan in an acidic environment and precipitation from solution when changed to an alkaline pH, allows the synthesis of magnetite nanoparticles and the *in situ* generation of a chitosan coating on their surface. Unfortunately, the resulting material, after crosslinking with epichlorohydrin, had low dispersibility in water and polar solvents, which was unfavourable from the point of view of biomedical applications [60]. I reasoned that the rearrangement of the hydroxyl groups of chitosan during the crosslinking process significantly weakened its hydrophilicity and that the addition of another polymer having a positive charge like chitosan should improve the dispersion of the nanoparticles.

To this end, I set out to design a polymer that, when mixed with chitosan would allow for improved dispersion of nanoparticles in polar solvents, but at the same time would allow the surface of the nanoparticles to be wetted by cyclohexane. I considered that a polymer containing both an aromatic ring and a quaternary ammonium salt in its structure should be suitable.

By free radical polymerisation, I obtained poly(bromide[*N-benzyl*-2-(methacryloxy)-N,*N-dimethylethanammonium*]) (PQ) (**Fig.2**) containing the aforementioned hydrophilic and hydrophobic units in its structure. This material had a solubility similar to that of chitosan: it dissolved in acetic acid solution and precipitated when the environment was alkalinised, allowing the use of the co-precipitation method in the synthesis of nanoparticles. Accordingly, I used the PQ

polymer in a mixture (1:1 and 5:1) with epichlorohydrin-crosslinked chitosan as a coating to stabilise the magnetite in the nanoparticles (results were published in articles **H1** and **A30**.). Article **H1** was included in a series of publications in pharmaceutical sciences submitted in 2015 by Dr Tomasz Siódmiak and concerning the kinetic racemic separation of ibuprofen with a 20% contribution from Dr Siódmiak (5 authors, my share 50%, 2015 submission) on the substantive scope concerning the immobilisation of *Candida rugosa* lipase (paragraphs 3.3 and 3.4 of the article) on the material designed, obtained and characterised by me.

The average size of the nanoparticles obtained ranged from 19 to 23 nm and was thus suitable for biomedical applications. The material also exhibited good thermal stability.

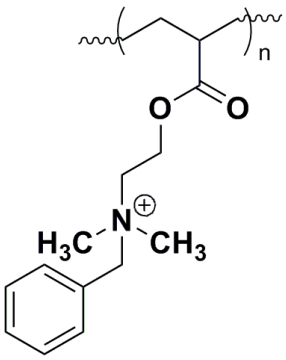

Fig.2. Structure of poly([*N*-benzyl-2-(methacryloxy)-*N*,*N*-dimethylethane ammonium bromide]) (PQ)

As expected, the chitosan-coated nanoparticles with the addition of the amphiphilic polymer PQ dispersed very well in polar and non-polar solvents (water, hexane, and toluene) without sedimentation. However, increasing the amount of PQ polymer to that of chitosan (5:1) resulted in a deterioration of the dispersion of the nanoparticles themselves.

Determining the number of reactive amine groups on the surface of the nanoparticles allows information to be obtained on the ability of the surface to react chemically [61,62]. Since I ultimately planned to use the obtained magnetic nanoparticles to bind drugs and blood serum proteins, the amount of free amine groups on the surface should be as high as possible. Unfortunately, after determining the number of primary amino groups using the ninhydrin method, it turned out that in the case of nanoparticles coated with chitosan and PQ polymer, their content on the surface significantly decreased in comparison with nanoparticles coated with pure chitosan cross-linked with epichlorohydrin (**3.73** mM/g) and was **2.5** mM/g for CS-PQ (1:1) and **0.7** mM/g for CS-PQ (1:5), respectively. I, therefore, concluded that the resulting material, despite very good dispersion in solvents with different dielectric constants would not allow a sufficiently large amount of serum protein to bind on its surface, which was confirmed in the test, I carried out (unpublished results).

However, it turned out that this arrangement has valuable advantages. As a result of research conducted by Dr Tomasz Siódmiak and Dr Dorota Chełminiak-Dudkiewicz as part of her PhD thesis, it turned out that such a number of amino groups, with an appropriate dispersion of nanoparticles, is nevertheless optimal for the catalytic activity of the enzyme deposited on the surface of the carrier, whereas too much amino groups led to its deactivation. The results of these studies by Dr Dorota Chełminiak-Dudkiewicz were included in her doctoral dissertation and were partly published in the fragment of publications **H2 and H5** on lipase immobilisation and in papers **A19-A21**, which are not part of my scientific achievement, so I will not discuss them further.

In the next stage of my work, I decided to test whether the type of crosslinking agent for the chitosan coating of the nanoparticles influences the amount of free amino groups on the surface of the material [**H7**]. For this purpose, I obtained magnetic nanoparticles coated with unmodified chitosan crosslinked traditionally with glutaraldehyde (**Fe_3O_4 -CS/Glu**). As mentioned, glutaraldehyde reacts during crosslinking with the free amino groups present in the deacetylated glucosamine unit of chitosan [55]. It would therefore be expected that the amount of free groups on the surface of nanoparticles coated with such a coating, compared to the material cross-linked with epichlorohydrin (**Fe_3O_4 -CS/Epi**), should be lower. The obtained **Fe_3O_4 -CS/Glu** nanoparticles had a size of 16 nm, thus comparable to **Fe_3O_4 -CS/Epi** nanoparticles and the number of free amine groups determined on their surface was **3.73** mM per gram of nanoparticles, which was identical to that obtained for **Fe_3O_4 -CS/Epi** [**H7**]. This allowed the preliminary conclusion **that the type of crosslinking agent for unmodified chitosan on the surface of magnetic nanoparticles does not affect the amount of free reactive amine groups on its surface**.

Between 2013 and 2015, I worked as the main investigator in the Ministry of Science and Higher Education's Iuventus Plus grant "Research on the potential use of saccharine dyes in modern materials chemistry", headed by Dr hab. Anna Kaczmarek-Kędziera. My research task involved, among other things, the synthesis of saccharine dyes by condensation of the corresponding amines with a squaric acid. The ease of bond formation between the squaric acid and amines, while at the same time being non-toxic to this compound, prompted me to try to use quaternary acid in the crosslinking of biopolymers containing primary amine groups. I proposed the use of this agent to Dr Joanna Skopinska-Wiśniewska for the cross-linking of collagen biomaterials obtained by her [63]. The idea proved successful, resulting in publication **A22**, which is not part of my scientific achievement. Based on the positive results with collagen, I decided to use squaric acid to crosslink chitosan on the surface of magnetic nanoparticles [**H5**]. Given that quaternary acid undergoes a condensation reaction with amine groups, one would expect a reduction in the content of free groups on the surface of the nanoparticles obtained in this way. I obtained nanoparticles coated with squaric acid cross-linked chitosan (**Fe_3O_4 -CS/SqA**) with a size of 20 nm and a content of free amino groups on the surface of the nanoparticles of **3.31** mM per gram of material, which is comparable with the

results obtained for previous materials. Based on the study and its results, I was able to definitively conclude that the **way in which the unmodified chitosan covering the magnetite core of the magnetic nanoparticles is cross-linked does not affect the number of free amino groups present on the surface of the material. It is therefore not possible to control this property of the nanoparticles by changing the crosslinking agent**. Therefore, it was necessary to find a solution to obtain magnetic nanoparticles with a suitably functionalised surface.

As part of the research published in paper **H5,** I also obtained collagen-coated nanoparticles cross-linked with squaric acid and a mixture of collagen and chitosan cross-linked in the same way. **An important conclusion from this work is the possibility of using quaternary acid to crosslink chitosan or biopolymer materials as a new and non-toxic agent.**

1.2 Nanoparticles coated with aminated chitosan (Fe_3O_4 -CSEt-$(NH_2)_n$)

Given that the purpose of the nanoparticles I designed and obtained was to bind a blood serum protein or a drug on their surface, I needed a material that would contain reactive functional groups on its surface allowing the deposition of as many of these ligands as possible. In the case of a protein, both the primary amino and and carboxyl groups present on the carrier [64,65]. Since chitosan already contains -NH_2 groups in its structure, which, among other things, give it a cationic character, I decided to continue to rely on this polymer. The addition of the amphiphilic polymer PQ did not yield the expected results, so I decided to chemically modify the chitosan to enrich it with free amino groups. For this purpose, I decided to use both the hydroxyl groups of chitosan and their reactivity as well as the amino group already present. Additionally, I considered that moving the newly formed amino groups away from the glycosidic unit should allow more of the protein to bind while retaining its activity due to less 'crowding' around the backbone of the macromolecule. As a result, I designed the structure of three modified chitosans containing one, two and three amino groups in the glycosidic unit (**Fig.3**).

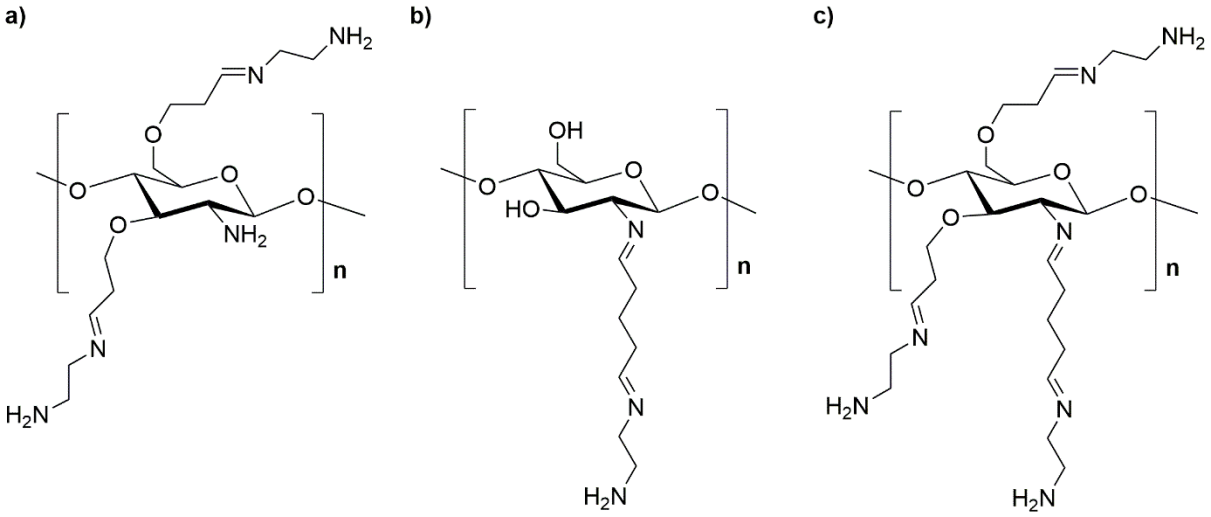

Fig.3. Designed structures of aminated chitosan **a)** Fe_3O_4 -CSEt-$(NH_2)_2$ **b)** Fe_3O_4 -CSEt-(NH_2) **c)** Fe_3O_4 -CSEt-$(NH_2)_3$

As the designed polymers were to have biomedical applications, I could not use aggressive and toxic reactants, but only those that had already been successfully used, for example for crosslinking biomaterials. Such conditions were met by epichlorohydrin, glutaraldehyde and ethylenediamine. Accordingly, I obtained three modified chitosans and coated magnetic nanoparticles. The results obtained were published in the articles **H2-H4** and **H7 and H8**.

1.2.1. Nanoparticles coated with modified chitosan with three amino groups in the glycosidic unit (Fe_3O_4-CSEt-$(NH_2)_3$) and its mixture with the amphiphilic polymer PQ

To functionalize the surface of magnetic nanoparticles with as many amino groups as possible capable of binding HSA, I first developed and optimized a method to synthesize aminated chitosan containing three amino groups per glycosidic unit (**CSEt-$(NH_2)_3$**). To this end, I carried out reactions leading to chitosan containing aldehyde groups using the reaction of glutaraldehyde with the amino group of the chitosan and epichlorohydrin with its hydroxyl groups. I confirmed the effectiveness of the modification and the achievement of the planned structure by solid state ^{13}C NMR spectroscopy [**H3**, **H4**]. The developed and optimised method for the synthesis of aminated chitosan was then applied to the surface modification of magnetic nanoparticles [**H2, H4**].

I obtained magnetic nanoparticles coated with pure, unmodified chitosan by co-precipitation and then functionalized the coating surrounding the magnetic core according to the developed procedure. I obtained nanoparticles coated with aminated chitosan with three amino groups in the glucosamine unit (**Fe_3O_4 -CSEt-$(NH_2)_3$**). The nanomaterial exhibited good dispersion in solvents of different polarity, and the nanoparticle size was 25 nm. Since the modification of chitosan was already

carried out on the surface of the magnetite core there was a risk of its oxidation to maghemite. Both the colour of the obtained nanoparticles and XRD analysis confirmed that the nanoparticles had a core made of magnetite.

The most relevant, from the point of view of my objective, was the content of primary amine groups on the surface of the nanoparticles, which I determined using the ninhydrin method. The obtained result of **8.34** mM per gram of **Fe** nanoparticles$_3$ **O$_4$ -CSEt-(NH$_2$)$_3$** indicated a high content of amine groups and was satisfactory. This mainly confirmed my belief, that my approach to solving the problem by increasing the number of groups capable of binding HSA was correct and that the modification carried out was effective. From the thermal analysis performed, it could also be deduced that the aminated chitosan **CSEt-(NH$_2$)$_3$** accounted for about 40 % of the nanoparticle mass [**H2, H4**].

Since the modified chitosan **CSEt-(NH$_2$)$_3$** and the nanoparticles coated with it contained a large number of free amine groups on the surface, I decided to check whether, in this case too, the addition of the ionic polymer PQ obtained by me would have a beneficial effect on the desired properties of the material. For this purpose, I prepared nanoparticles coated with a mixture of **CSEt-(NH$_2$)$_3$** and PQ in mass ratios of 1:1 and 1:5 [**H3**], similarly to the for nanoparticles coated with a mixture of unmodified chitosan and the same cationic polymer [**H1**]. The obtained nanoparticles had an average size of 20 to 25 nm, and XRD analysis confirmed that the core was made of magnetite. Based on the thermal analysis of the nanoparticles obtained, it could be proven that the proportion of the material constituting the polymer coating of the nanoparticles was approximately 30 wt%. When the content of amino groups was determined, it turned out that the surface contained 2.5 mM of these groups per gram of material, which was like that of nanoparticles coated with a mixture of unmodified chitosan and PQ polymer. This meant that the **addition of the PQ polymer reduces the number of free amine groups available on the surface of the nanoparticles, which is unfavourable for the material to be used as a carrier for HSA**.

As I have already mentioned, the addition of PQ proved to be very beneficial when using the materials I designed as a carrier for lipase, however, these studies and their result are not the subjects of my Achievement. Considering the results obtained, I finally decided to abandon the synthesis of magnetic nanoparticles with the addition of the ionic polymer PQ and focus on further modification of chitosan.

1.2.1. Chitosan-coated nanoparticles with one (Fe_3O_4-CSEt-(NH_2)) and two amino groups in the glycosidic unit (Fe_3O_4 -CSEt-(NH_2)$_2$)

Obtaining **CSEt-(NH$_2$)$_3$** aminated chitosan and coating magnetic nanoparticles with a high content of free amino groups on the surface prompted me to carry out two further modifications of chitosan. I focused on obtaining a polysaccharide with one (**CSEt-(NH$_2$)**) and two amino groups in the glycosidic unit (**CSEt-(NH$_2$)$_2$**), and

coating magnetic nanoparticles with them [**H4**, **H7**]. Obtaining these materials was aimed at clarifying whether it would be possible to engineer the surface of the nanoparticles in such a way that their properties could be controlled.

I have synthesised chitosan containing one amino group offset from the glucosidic ring of **CSEt-(NH_2)** by modifying the amino group of chitosan with glutaraldehyde, followed by the subsequent reaction of the with ethylenediamine. In the case of chitosan with two amino groups **CSEt-(NH_2)$_2$** I carried out the reaction of the hydroxyl groups of the starting polysaccharide with epichlorohydrin and ethylenediamine. All the reactions carried out leading to both **CSEt-(NH_2)** and **CSEt-(NH_2)$_2$** were repetitions of the methods I used to synthesise **CSEt-(NH_2)$_3$** , so they did not require optimisation of conditions. I confirmed the structure of the obtained materials by solid state ^{13}C NMR spectroscopy [**H4**] and ATR FT-IR analysis [**H4**, **H7**]. I also investigated the thermal stability of the obtained chitosans, the results of which were puzzling in the case of the material **CSEt-(NH_2)$_2$**. It turned out that, despite prolonged drying under vacuum at 50° C, it was not possible to get rid of the water present in the sample. Even after drying to a constant weight, it was found by TG and DTG analysis that this modified chitosan still contained about 30% moisture. Furthermore, the thermal decomposition in the modified chitosan **CSEt-(NH_2)$_2$** occurred differently than in **CSEt-(NH_2)** and the previously obtained **CSEt-(NH_2)$_3$** . This turned out to be the first signal suggesting that this material deviates in its properties from the others, which I will write about in more detail when discussing the results published in paper **H7**.

After ensuring that I obtained my designed modified polymeric materials, I synthesised the coated magnetic nanoparticles, obtaining **Fe_3O_4 -CSEt-(NH_2)** and **Fe_3O_4-CSEt-(NH_2)$_2$** nanomaterials, respectively. These nanoparticles were characterised by a size range from 22 to 25 nm. Determination of the amount of free amine groups on their surface made it possible to assess whether the engineered material structure has a direct bearing on this property of the nanoparticles. The amount of free amine groups on the surface of nanoparticles coated with modified chitosan containing one amine group moved away from the glycosidic ring (**Fe_3O_4 -CSEt-(NH_2)**) was **3.15** mM per gram of material, and in nanoparticles coated with chitosan with two amine groups - **5.5** mM/g. This confirmed my assumption that **by chemical modification of the surface of magnetic nanoparticles, their properties can be controlled**. By designing the surface of magnetic nanoparticles in this way, I was able to obtain a sequence of three materials with increasing contents of free, reactive groups on the surface: **Fe_3O_4 -CSEt-(NH_2)** - 3.15 mM/g, **Fe_3O_4 -CSEt-(NH_2)$_2$** - 5.5 mM/g and **Fe_3O_4 -CSEt-(NH_2)$_3$** containing 8.34 mM/g NH_2 groups .

Based on the thermal analysis performed, the polymer coating accounted for approximately 30-35% of the nanoparticle mass. In addition, analysis of the curve TG -DTG showed that the magnetic material coated with modified chitosan with two amino groups **Fe_3O_4-CSEt-(NH_2)$_2$** contained significantly more bound moisture than the other nanoparticles **Fe_3O_4-CSEt-(NH_2)** and **Fe_3O_4-CSEt-(NH_2)$_3$** and that its thermal degradation occurs in a different manner than in the other derivatives. These

differences proved to be quite important in my further research on the evaluation of the materials' ability to bind HSA [**H7**].

1.3 Magnetic nanoparticles coated with aminated starch (Fe_3O_4 -AS); development of fast and solvent-free amination method

Next to the chitosan, I used to stabilise the magnetite core, starch is the second most widely used in biomedical science and pharmaceutical sciences a biocompatible and biodegradable polysaccharide [66-68]. The presence of hydroxyl groups and, above all, the rather good solubility of starch make it frequently modified by simple chemical reactions. Obviously, the properties of starch depend on its source and thus its amylose and amylopectin content.

There are no free amine groups in the starch structure, however, based on my experience in the synthesis of oxidised starch to dialdehyde starch [69], which I published in article **A17** not part of the scientific achievement, I decided to obtain aminated starch (Fig.4) using the reaction of aldehyde groups with ethylenediamine, which I had successfully used in the modification of chitosan, and then to obtain magnetic nanoparticles coated with it.

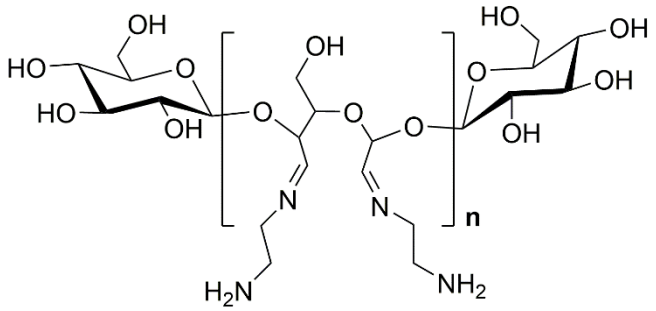

Fig.4. Structure of aminated starch (**AS**)

As with the first modification of chitosan to **CSEt-(NH_2)$_3$,** I first optimised the conditions for the synthesis of the polymer itself. As I mentioned, obtaining aminated starch required the prior oxidation of starch to dialdehyde starch. Based on the results obtained in publication **A13**, I chose maize starch as the starting material and then oxidised it with sodium periodate. This yielded dialdehyde starch (**DAS**) with an oxidation degree of glycosidic units of 68% [**A17**, **H6**]. The next step to obtain aminated starch was the reaction of **DAS** with ethylenediamine. Initially, I carried out this reaction analogously to the chitosan modification - in carbonate buffer for 2 hours. I obtained an aminated **AS** starch, the structure of which I confirmed by ^{1}H NMR spectroscopy. Although the synthesis was successful, the procedure for separating the aminated starch from the reaction mixture has considerable preparative limitations, requiring the use of a considerable amount of acetone for

precipitation from the buffer. Of course, this problem would certainly be minimised with the modification of the starch-coated nanoparticles, as the reaction would be carried out on the surface of insoluble material, but the desire to reduce the number of reagents and solvents used led me to look for another solution.

While still working on my PhD thesis involving the synthesis of boronated amino acids, I became interested in mechanochemical synthesis methods involving grinding the reactants in a mortar, without using a solvent. Reactions of this type make it possible to shorten reaction times and reduce the number of reactants and, above all, solvents, which is in line with the trend towards *green chemistry* [70,71]. As part of the research described in my PhD thesis, I developed a very efficient method for the iodination of hydantoin 2-indanone precisely by using grinding in a mortar. The problem I was trying to solve at the time was very similar to the one I encountered in the synthesis of aminated starch - large amounts of solvents that could not be recovered after synthesis. It was for this reason that I decided to try to carry out the amination reaction of dialdehyde starch by running the with ethylenediamine. I monitored the progress of the reaction by ATR FT-IR analysis, where, after one minute of mashing, I no longer observed the bands characteristic of the aldehyde groups, indicating that the DAS had overreacted. The structure of the resulting aminated starch (AS) was also confirmed on the ^{1}H NMR spectrum. **I have** therefore **developed a fast and efficient method for the amination of aldehyde polymers by grinding the reactants in a mortar, without solvent**.

I was now able to use such optimised synthesis conditions to obtain the designed magnetic nanoparticles. In the first step, I obtained starch-coated nanoparticles (**Fe_3O_4-S**) by precipitating the nanoparticles from a starch solution. The starch covering the magnetic core of the **Fe_3O_4-S** nanoparticles was oxidised under the conditions developed for the pure polymer, resulting in **Fe_3O_4-DAS** nanoparticles. XRD analysis confirmed that the oxidation reaction occurred only on the surface of the nanoparticles and the core was still magnetite. The final step in the synthesis was to use the amination method I developed by grinding in a mortar. I ground the **Fe_3O_4-DAS** nanoparticles with ethylenediamine for 1 min, obtaining designed magnetic nanoparticles coated with aminated **Fe_3O_4-AS** starch. The results of the XRD analysis again confirmed that in this case also the core of the nanoparticles was magnetite. I was therefore able to conclude that the **amination by grinding method I developed could be used to functionalise the surface of magnetic nanoparticles**.

The resulting magnetic nanoparticles coated with aminated starch **Fe_3O_4-AS** had a diameter of 25 nm and the determined amount of free amino groups on their surface was **5.63** mM per gram of nanoparticles [**H6**], which is very close to the value obtained for nanoparticles coated with modified chitosan with two amino groups in the glucosamine unit - **5.5** mM/g [**H4, H7**]. Based on thermal analysis, it was found that the polymer coating covering the magnetite core in **Fe_3O_4-AS** nanoparticles accounted for about 20% of the nanoparticle mass. Despite the similar

content of amino groups as in **Fe_3O_4-CSEt-$(NH_2)_2$**, the moisture content of the obtained **Fe_3O_4-AS** nanoparticles determined from the TG-DTG curve was only 5%.

Since the synthesis of the magnetic nanoparticles I obtained coated with modified chitosans (**Fe_3O_4-CSEt-$(NH_2)_{n=1,2,3}$**) was analogous in the last step to that of **Fe_3O_4-AS**, I decided to check whether the solvent-free amination method I had developed would also work in this case [**H7**, **H8**]. To this end, I modified the magnetic core-covering chitosan according to the procedure described in publications **H2-H4** until chitosans containing aldehyde groups in the ring were obtained. After separating the nanoparticles with a magnet and drying them, I ground them in a mortar with ethylenediamine for 1 minute. As expected, I obtained **Fe_3O_4-CSEt-(NH_2)**, **Fe_3O_4-CSEt-$(NH_2)_2$** and **Fe_3O_4-CSEt-$(NH_2)_3$** nanoparticles with diameters of 22, 25 and 29 nm, respectively, and thus identical to those using the classical amination method. The content of free amine groups on the surface was also similar: 3.25; 5.93 and 8.34 mM per gram of material [**H7**]. The results obtained confirmed that the **solvent-free and rapid amination reaction method** I developed **is effective. Importantly, it allows for efficient functionalization and control of the surface properties of the polymer coating surrounding the magnetite nanoparticle core**.

In the next stage of my research, I confirmed the ability of the nanoparticles I obtained coated with polysaccharides and their modified derivatives to immobilise HSA on their surface.

2. Binding of human serum albumin on the surface of magnetic nanoparticles; effect of material synthesis and drying conditions on immobilisation efficiency

Human serum albumin (HSA) is one of the most important proteins found in plasma [72]. It is composed of 585 amino acid residues organised in three domains forming a polypeptide that resembles the shape of a heart. One of the primary roles of HSA is its ability to bind substances including drugs [73-75]. The active substance bound to albumin is pharmacologically inactive, so it is very important to study drug interactions specifically with this protein.

Working with protein material due to the formation of colloidal solutions is difficult. Isolating HSA from the supernatant requires techniques such as ultrafiltration, ultradialysis or microcentrifugation, which are time-consuming and do not always allow the separation of all the protein used for the study. A solution could be to deposit HSA on a carrier that would allow rapid and efficient isolation of the material from solution. A prerequisite for the carrier is that it binds the protein while retaining HSA activity after immobilisation.

The binding of a protein to the surface of a carrier containing amino groups can be carried out in two ways: by activating the surface of the carrier with glutaraldehyde and reacting with the amino groups of the protein, or by activating the carboxyl groups of the protein with EDC and sulfo-NHS and then reacting

with the amino groups of the carrier. The most used and effective method for binding proteins to a carrier is the use of an EDC/sulfo-NHS binding agent.

As I have used two amination reaction methods when synthesising magnetic nanoparticles coated with modified polysaccharides: the traditional one in a solvent and the one I developed by grinding in a mortar, this time I decided to see if this would affect their ability to bind HSA. For this purpose, I chose model nanoparticles coated with aminated chitosan (**Fe_3O_4-CSEt-(NH_2)$_{n=1,2,3}$**), since the polymer coating was formed by modifying the same starting polysaccharide. Furthermore, given the problem of removing moisture from a material containing two amine groups (**Fe_3O_4 - CSEt-(NH_2)$_2$**) I found it worthwhile to use freeze-drying of the nanoparticles in addition to vacuum drying. Finally, I carried out HSA immobilisation on the surface of nanoparticles coated with aminated chitosans (**Fe_3O_4-CSEt-(NH)$_{2n=1,2,3}$**) using activation of the carboxyl groups of the protein with EDC/sulfo-NHS [**H7**].

The results obtained were in some ways surprising to me. I had expected that the amount of surface-bound HSA nanoparticles would increase with an increase in the number of amine groups on the carrier. Meanwhile, this proved to be true only for **Fe_3O_4-CSEt-(NH_2)** and **Fe_3O_4-CSEt-(NH_2)$_3$** materials while chitosan-coated nanoparticles with two amino groups showed very low HSA-binding capacity regardless of their synthesis method and the way the material was dried. It was observed that for all nanoparticles, the amount of bound HSA increased for materials subliminally dried in a freeze-dryer and obtained in the last step by a solvent-free method [**H7**].

Given that the highest amount of albumin bound on the surface of **Fe_3 O_4 - CSEt-(NH_2)$_2$**, obtained without solvent and dried in a freeze dryer, was only 25.7 mg per gram of nanoparticles, I concluded that the geometry of the modified chitosan might be the cause. I surmised that the amino groups must be spatially aligned in this material so that a kind of spatial hinge is created preventing the binding of albumin. Given that this material was already differentiated from other modified chitosans and coated nanoparticles [**H4**], I decided to clarify this issue based on theoretical calculations. I asked Dr hab. Anna Kaczmarek-Kędziera from the Faculty of Chemistry of the UMK and Dr Mariana Kozłowska from the Institute of Nanotechnology Karlsruhe to perform molecular dynamics simulation calculations in water for the **CSEt-(NH_2)$_{n=1,2,3}$** aminated chitosans I obtained. The simulations confirmed my assumption that the **CSEt-(NH_2)$_2$** polymer exhibits a spatial structure different from that of other materials.

After visualisation of the results, it could be seen that the chain of this aminated chitosan, in comparison with **CSEt-(NH_2)** and **CSEt-(NH_2)$_3$** , is characterised by a rather high flexibility and a tendency to form intramolecular hydrogen bonds between the introduced amino groups and the hydroxyl groups present in the glucosamine ring with hydroxyl groups. This was most likely influenced by the previously observed relatively high amount of moisture that was difficult to remove from this material [**H4**] and the inaccessibility of the amino groups to the activated albumin. **The geometry of the polymer covering the core of**

the nanoparticles, therefore, has a significant impact on their reactivity and availability to bioligands such as HSA.

In the next stage of my research, I decided to address the question of the content of the amino groups once again. The initial criterion I adopted was related to the possibility of controlling the ability of magnetic nanoparticles to bind HSA. To this end, I carried out HSA immobilisation on the surface of selected nanoparticles differing in the content of free amino groups on the surface and, in the case of nanoparticles coated with unmodified chitosan, with a different crosslinking agent. Given the results obtained, I decided to use only the aminated nanoparticles that I obtained by grinding in a mortar for comparison. I dried all materials by freeze-drying. For some of the nanoparticles, I also used both HSA immobilisation methods (glutaraldehyde; EDC/sulfo-NHS) to compare their efficiency. I confirmed the activity of albumin bound on the surface of the nanoparticles with an anti-HSA test, which is a standard method to check whether the modified protein retained its ability to bind the substance. The results obtained are presented in Table 1.

As can be seen, the amount of bound human blood serum albumin on the surface of the magnetic nanoparticles I obtained increases as the number of available amino groups on the surface of the magnetic nanomaterial increases. The exception is the nanoparticles **Fe_3O_4-CSEt-$(NH_2)_2$**, which is explained in detail. In the case of nanoparticles coated with unmodified chitosan, the use of squaric acid as a crosslinking agent slightly improved the ability of the carrier to bind HSA.

Table 1. Amount of human serum albumin bound on the surface of magnetic nanoparticles with different contents of free amine groups

Nanoparticles	Number of NH_2 groups on the surface [mM/g]	Amount of bound HSA [mg/g]		Publication
		Activation by glutaraldehyde	Activation EDC/sulfo-NHS	
Fe_3O_4-CS/Glu	3.73	35.5	75.6	**H8**
Fe_3O_4-CS/SqA	3.31	-	79.2	**H8**
Fe_3O_4-CSEt-(NH_2)	3.15	76.8	150.0	**H7,H8**
Fe_3O_4-CSEt-$(NH_2)_2$	5.93	-	25.7	**H7**
Fe_3O_4-CSEt-$(NH_2)_3$	8.34	98.4	210.3	**H2,H7,H8**
Fe_3O_4-AS	5.63	150.0	165.3	**H6,H8**

The results obtained and interpreted allows concluding that **it is possible to control the ability of magnetic nanoparticles to bind bioligands by optimising the polysaccharide coating covering the magnetite core**.

2.1 Use of magnetic nanoparticles with immobilized HSA to study the extent of albumin binding to ketoprofen [H8].

The property of human serum albumin (HSA) to bind and storage of ligands, which may include drugs, is one of its most important characteristics. As HSA accounts for approximately 50 per cent of plasma mass, it's binding of active substances is an important pharmacokinetic factor affecting drug efficacy and distribution. The formed HSA-drug complex, due to its large size, does not diffuse from the vascular compartment into the tissue and thus cannot reach the correct receptor. Therefore, it is important to study the drug-HSA interaction of both known and newly introduced therapeutic substances. Since most inflammatory and pathological conditions in the body are accompanied by oxidative stress, it is important to study the HSA-drug interaction under both normal and oxidative stress conditions. Reactive oxygen species in oxidative stress affect structural changes in the HSA molecule, leading to its oxidised form characterised by a different ability to bind ligands [76,77]. Studying the interaction of HSA with drugs, to determine its degree of binding, requires techniques that allow the separation of the HSA-drug complex from the supernatant such as ultrafiltration, ultracentrifugation or microdialysis.

Deposition of HSA on magnetic nanoparticles while retaining the ability of albumin to interact with the drug, and the use of such a system to determine the degree of binding of active substances would significantly improve the quality of work and efficiency of separation of the HSA-drug complex from the supernatant. As the nanoparticles I obtained allowed the binding of a sufficiently large amount of HSA without losing its activity confirmed by the anti-HSA test, I decided to use them to determine the interaction with ketoprofen, which I chose as a model OTC NSAID drug. I studied the interaction both under normal conditions and after artificially induced oxidative stress. This research was the focus of the NSC Sonata 8 grant (**2014/15/D/NZ7/01805)** entitled *Synthesis and study of the interaction of magnetic nanoparticles coated with human serum proteins with selected drugs under normal and artificially induced oxidative stress conditions, of* which I was the director from 2015-2019.

As HSA carriers, I chose magnetic nanoparticles with increasing amino groups on the surface, for which I had previously investigated the effect of the synthesis and drying method on the binding capacity of HSA (Table 1) [**H8**]. I replaced the chitosan-coated nanoparticles with two amino groups by nanoparticles coated with aminated starch (**Fe_3O_4-AS**), as these contained almost the same amount of amino groups on the surface as the excluded material. The oxidative stress inducers I used under laboratory conditions were hydrogen peroxide, the hydroxyl radical generated by the Fenton reaction and chloramine-T. For comparison, I also performed tests under similar conditions for native HSA - not immobilised on the carrier.

The obtained results confirmed that albumin embedded on magnetic nanoparticles retained its ability to interact with drugs and the amount of bound ketoprofen was comparable to the results for free HSA [**H8**]. Furthermore, the type of nanoparticles used as carriers did not affect the ability of the protein to interact with ketoprofen or the amount of bound drug. Furthermore, I separated the magnetic nanoparticles with the HSA-drug complex on the surface after the interaction study in a simple and efficient way by decanting the supernatant after applying the magnet (Fig.1). For the oxidative stress interaction study, HSA oxidised on the surface of the nanoparticles similarly to native oxidised HSA bound less drug than before the stress, which is in line with general knowledge of pharmacokinetics. The amount of bound ketoprofen did not depend on the type of carrier, but, as expected, on the stress-inducing agent. The correctness of the results obtained was confirmed by an example of the ketoprofen binding isotherm determined for **Fe_3O_4-AS-HSA** nanoparticles**.**

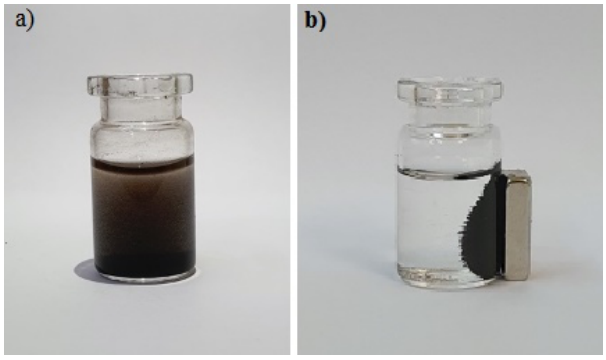

Photo.1. Magnetic nanoparticles with immobilised albumin in ketoprofen solution before (**a**) and after magnet application (**b**), [H8].

The results published in paper **H8** indicated that the **magnetic nanoparticles I obtained, with human serum albumin bounded on their surface, could be used to determine the basic pharmacokinetic parameters of drugs *in vitro* under both normal and oxidative stress**. Furthermore, the presence of the magnetic core did not enhance the oxidative effect of oxidative stress on albumin deposited on the nanoparticles. The results obtained from my research open new possibilities in pharmaceutical analysis and biotechnology due to the ease of working with magnetic material.

3. Levane- and photosensitiser-coated magnetic nanoparticles as a potential new drug formulation for photodynamic PDT therapy [H9]

In the final stage of my research related to the preparation of new magnetic nanoparticles coated with polysaccharides, I decided to use in the synthesis a polysaccharide with which they have so far never been coated - levan. Levan is a polyfructan (Fig.3) produced by living organisms such as some plants, bacteria, or fungi [78,79].

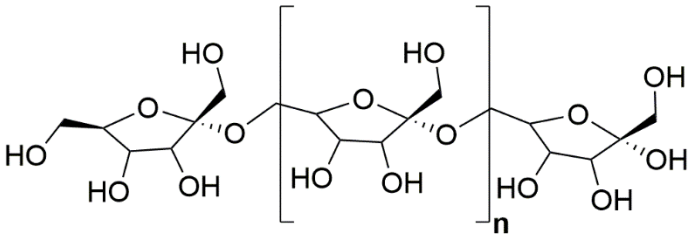

Figure 5: Levan structure

Like the chitosan or starch I used earlier, levan is a non-toxic, biocompatible, and biodegradable polysaccharide. Its characteristic feature is its ability to form adhesive bonds with many substances, which has found applications in cosmetics as well as the food industry. Recent literature reports also mention the anticancer effect of bacterial levane, which may be due to its antioxidant properties. It should therefore be an ideal material to stabilise the magnetite core and prevent its oxidation.

I prepared magnetic nanoparticles coated with levan (**Fe_3O_4-Lev**) by co-precipitation, taking advantage of the fact that, like chitosan, it dissolves in an acidic medium and remains insoluble in solutions of alkaline pH. Furthermore, due to the lack of groups in the levan structure that could provide cross-linking between the polysaccharide chains, I used epichlorohydrin as a cross-linking agent. The nanoparticles obtained were approximately 15 nm in diameter and had good dispersion in polar solvents and did not aggregate [**H9**].

However, my aim was to obtain a material that could find biomedical applications, and the binding of HSA on the surface of the obtained **Fe_3O_4 -Lev** nanoparticles would require modification of the polysaccharide. During my research, I also began to be interested in the use of polymeric materials as photosensitising carriers for photodynamic therapy [80-82]. This resulted in exploiting the ability of levan to form adhesive bonds with various chemicals and drugs and attempting to deposit them on the surface of the resulting nanoparticles. I was interested in investigating to what extent the free radical scavenging ability of levan would affect the photosensitising activity. Furthermore, simply combining the photosensitiser with a carrier containing a magnetite core capable of generating reactive oxygen species, which is its disadvantage, could have yielded surprising results.

I chose zinc (II) phthalocyanine (**ZnPc**), which has been used clinically in photodynamic therapy (PDT), as a model drug [83,84]. A limitation in the use of this drug, however, is its highly hydrophobic nature resulting in poor distribution and a strong tendency to aggregate in body fluids. Deposition of this drug on magnetic nanoparticles coated with hydrophilic levane should lead to a new formulation of the drug with less tendency to aggregate. Of course, a prerequisite was the retention of phthalocyanine activity, which in the case of a photosensitiser is the ability to generate singlet oxygen.

Magnetic nanoparticles coated with levan and ZnPc (**Fe_3O_4-Lev-ZnPc**) were obtained by adding to the levan solution dissolved phthalocyanine in dimethylformamide, followed by co-precipitation of the nanoparticles and the surrounding core shell. From the analysis of the TG-DTG curves, it can be estimated that the levane accounted for about 21% of the nanoparticle mass and the deposited drug only 3%. The size of the **Fe_3O_4-Lev-ZnPc** nanoparticles**, due to the** small addition of the drug, did not change compared to nanoparticles coated with levan alone. The resulting nanoparticles exhibited good dispersion in polar solvents and did not aggregate, suggesting the hydrophilic nature of the **Lev-ZnPc** coating covering the magnetite core. This was confirmed by measuring the wetting angle of the **Lev-ZnPc** system. **Thus, a form of the drug was obtained with enhanced dispersion and no tendency to aggregate,** which is highly beneficial for its pharmacokinetics.

The ability of the ZnPc drug to generate singlet oxygen is a measure of its pharmacological activity. To definitively confirm that a new formulation of this drug had been successfully obtained, I had to prove that the photosensitiser retained its activity. The literature quantum yield of singlet oxygen generation for pure zinc phthalocyanine is about 0.56. For the compound to be used as an effective photosensitiser in photodynamic therapy, this yield should be at least 0.3. For the **Fe_3O_4 -Lev-ZnPc** nanoparticles I obtained, the experimentally determined singlet oxygen generation yield using LED radiation was on average 0.41, which is 71% of the yield of pure zinc phthalocyanine. However, this is the amount of singlet oxygen that allows for the clinical use of the drug. Considering that **the new drug formulation obtained by me** in the form of **Fe_3O_4 -Lev-ZnPc** magnetic nanoparticles **has higher dispersion in polar solvents, exhibits hydrophilic character and does not aggregate, and the drug at 3 wt.% relatives to the carrier retained 71 % of its activity,** I believe that the developed drug formulation is very promising, and the subject matter is developmental. Magnetic nanoparticles coated with levan, which has proven anticancer activity, in combination with drugs used in cancer therapy could be the basis for obtaining selective and effective forms of these drugs with improved pharmacokinetic parameters.

The results published in the **H9** article, on the one hand, conclude my series of works on the optimisation of the polysaccharide coating of magnetic nanoparticles with biomedical applications and, on the other hand, show the direction of the

research I am currently carrying out and which, in collaboration with specialists in the specialists in the field of phytopharmacology I intend to develop further.

4. A summary of the results of the research constituting the scientific achievement and its possible use

The subject of the research presented in the publications constituting the Scientific Achievement is related to the design and synthesis of new magnetic nanoparticles with a polysaccharide coating optimised towards biomedical applications. The publication series **H1-H9** deals with the very topical and strongly developing topic of synthesis and applications of multifunctional nanomaterials. As part of my research, I obtained and fully characterised fifteen types of novel polysaccharide-coated magnetic nanoparticles, which also required me to first obtain the polymer coatings themselves to optimise the synthesis method. In publication **H1,** these were nanomaterials coated with chitosan and its mixture with an ionic polymer. Papers **H2-H4** dealt with the synthesis of novel aminated chitosans and magnetic nanoparticles coated with them. In paper **H5,** I presented the preparation of nanoparticles coated with a mixture of chitosan and collagen using crosslinking of the coating covering the magnetic core with a new crosslinking agent quaternary acid. Single-author publication **H6** concerned the synthesis of nanoparticles coated with aminated starch and the development of a rapid amination method in the *green chemistry* stream. The levane-coated nanoparticles presented in paper **H9** were the last material I included in the presented achievement.

In addition to the synthesis and characterisation of the obtained materials, I used them as effective carriers for human serum albumin (HSA) in publications **H2**, **H6**, **H7**, and **H8**, as well as a clinically used photosensitiser - article **H9**. I used the obtained nanoparticle-HSA systems to determine the degree of binding of a model drug to HSA under normal and artificially induced oxidative stress conditions - publication **H8**. In addition, I systematically analysed the influence of factors such as the method of synthesis or the geometry of the polysaccharide covering the magnetic core on the ability of the carrier to bind HSA - publication **H7**.

The results of the research contained in articles **H1-H9** that form the basis of the presented scientific achievement can be summarised as follows:

- **Novel magnetic nanoparticles with magnetite-based core** coated with chitosan [**H1**, **H5**], chitosan and ionic polymer [**H1**], aminated chitosan containing one, two and three amino groups in the glucoside unit [**H2**, **H3, H4**, **H7**, **H8**], a mixture of aminated chitosan and ionic polymer [**H3**], aminated starch [**H6**, **H8**] and levan [**H9**],
- **A new ionic polymer** poly([*N*-benzyl-2-(methacryloxy)-*N,N*-dimethylethane ammonium bromide]) **was designed for structure, prepared and characterised.** [**H1**, **H3**], and it was also shown that the addition of the ionic

polymer in the coating covering the magnetic nanoparticles improves the dispersion of the nanoparticles in polar and non-polar solvents, but reduces the content of free amine groups on their surface [**H1**, **H3**],

- **modification of chitosan towards three new polymers with increasing amounts of free amino groups in the glucosamine unit CSEt-$(NH_2)_{n=1,2,3}$ [H2**, **H3**, **H4**, **H7**], and the modification conditions of chitosan towards its aminated derivatives **CSEt-$(NH_2)_{n=1,2,3}$** for the synthesis of **Fe_3O_4-CSEt-$(NH_2)_{n=1,2,3}$** magnetic nanoparticles **[H2**, **H3**, **H4**, **H7**] were also applied,
- it was shown that an appropriately designed chemical modification of the polysaccharide and polysaccharide coating of the magnetic nanoparticles controlled the number of free amino groups on the surface [**H2**, **H4**, **H7**], and it was found that the aminated chitosan containing two amino groups **CSEt-$(NH_2)_2$** and the **Fe_3O_4-CSEt-$(NH_2)_2$** coated magnetic nanoparticles showed a high tendency to bind difficult to remove moisture [**H4**],
- the effect of the geometry of the modified chitosan molecule on its properties was investigated [**H7**],
- effectively used non-toxic squaric acid to crosslink chitosan on the surface of magnetic nanoparticles [**H5**],
- modification of starch to dialdehyde and aminated starch was carried out [**H6**],
- **a new, fast and solvent-free method for amination of an aldehyde polysaccharide by grinding in a mortar was developed [H6] and applied to modify the polysaccharide coating of magnetite nanoparticles** [**H6**, **H7**, **H8**],
- controlled the properties of the resulting magnetic nanoparticles by selecting the drying method and the method of synthesis: in or without solvent [**H7**],
- **human serum albumin (HSA) was covalently bound on the surface of the obtained nanoparticles, its activity was confirmed** [**H2**, **H6, H7**, **H8**], and it was shown that the amount of bound HSA on the surface of magnetic nanoparticles depends on the number of free amino groups on the surface of the carrier; the larger the more albumin immobilised [**H7**, **H8**],
- it was found that due to the flexibility and ability of aminated chitosan **CSEt-$(NH_2)_2$** to form intra-chain hydrogen bonds, magnetic nanoparticles coated with this polymer are not suitable as a carrier for the efficient immobilisation of HSA despite the high content of amino groups on their surface [**H7**],
- **used magnetic nanoparticles with surface-bound HSA to study the interaction of albumin with the model drug ketoprofen under normal and artificially induced oxidative stress conditions** [**H8**].

Furthermore, it has been shown that:

- *in vitro oxidative* stress inducers such as hydrogen peroxide, hydroxyl radical and chloramine-T induced oxidative changes in the structure of HSA immobilised on magnetic nanoparticles analogous to that of native HSA [**H8**],

while artificially induced oxidative stress did not cause changes in the magnetic core structure of the nanoparticles [**H8**],

- the binding capacity of HSA immobilised on the resulting magnetic nanoparticles was comparable to the results obtained for native HSA under both unstressed and oxidative stress conditions [**H8**], whereby HSA immobilised on the surface of magnetic nanoparticles can be used to determine the basic pharmacokinetic parameters of drugs, which is significant facilitation of the procedure for studying protein interactions [**H8**],
- **magnetic nanoparticles coated with levan and clinically used in PDT zinc phthalocyanine, were obtained** [**H9**],
- Zinc phthalocyanine retained its photosensitising activity when deposited on the surface of levan-stabilised magnetic nanoparticles [**H9**], and, in addition, the pharmaceutical formulation of zinc phthalocyanine on the surface of levan-coated magnetic nanoparticles had better dispersion, hydrophilicity and lack of aggregation compared to pure zinc phthalocyanine [**H9**],
- Levane-coated magnetic nanoparticles can provide a carrier for new formulations of clinically used drugs to improve their pharmacokinetic parameters [**H9**].

The results presented as part of the scientific achievement were cognitive in nature but have considerable application potential. This is evidenced by the fact that the materials obtained by me have been used in biocatalysis, ligand uptake techniques, enantioselective drug preparation and for interactions in thin films with a model biological membrane, and that they formed an important part of the research carried out by the other co-authors of the publications I have included in the list of articles unrelated to my Scientific Achievement.

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5. Presentation of significant scientific or artistic activity carried out at more than one university, scientific or cultural institution, especially at foreign institutions

5.1 Scientific activities carried out in cooperation with centres from Poland

My scientific interests in medicinal chemistry and pharmaceutical chemistry, and a desire to further develop in this area, has led to collaborations with research groups involved in the synthesis and analysis of medicinal substances.

Long-standing cooperation with the team of Prof. Dr Michał Marszałł (Chair and Department of Drug Chemistry, Faculty of Pharmacy, Collegium Medicum L. Rydygier in Bydgoszcz) involved the use of magnetic nanoparticles synthesised by me in pharmaceutical analysis and as carriers of biocatalysts. The cooperation, which continues to this day, resulted in publications included in scientific achievements **H1, H2, H5, H8** and **H9**, as well as side articles **A13**, **A19-A21**, **A25 and** one obtained patent **PL No 227525 B1**. Our collaboration also included the implementation of two grants from NCN: SONATA 8 entitled. "*Synthesis and study of the interaction of magnetic nanoparticles coated with human blood serum protein with selected drugs under normal and artificially induced oxidative stress conditions"* (2014/15/D/NZ7/01805, 2015-2019), of which I was the director and Dr Tomasz Siódmiak one of the contractors, and OPUS 8 (2014/15/B/NZ7/0097) titled "Synthesis, characterisation and evaluation of *magnetic nanoparticles coated with human blood serum protein with selected drugs under normal and artificially induced oxidative stress conditions". "Synthesis, characterisation and activity evaluation of biopolymer-modified magnetic nanoparticles as potential enzyme carriers in the synthesis of beta-blocker drugs*" which was led by Prof. Michał P. Marszałł, Ph.D., and I acted as a contractor. In 2019, together with the teams of Prof. Dr. Michał Marszałł, Dr. Bogumiła Kupcewicz Prof. UMK (CM UMK in Bydgoszcz) and Prof. Andrzej Wojtczak, PhD, and Prof. Iwona Łakomska, PhD, from the UMK Faculty of Chemistry, we formed an interdisciplinary research team called BRAIN (Biomedical and phaRmAceutical InterdidcipliNary group) within the UMK Excellence Initiative, which was recognised as a priority research team and at the same time included in the Toruń Centre of Excellence 'Towards personalised medicine".

Another research group from the area of pharmaceutical sciences with which I have established fruitful cooperation, continuing to this day, is the team of Prof Tomasz Gośliński, who heads the Department of Chemical Technology of Medicinal Products at the Karol Marcinkowski Poznań Medical University. Research conducted by Prof. Tomasz Gośliński's team in synthesis of photoactive compounds, combined with my experience in the synthesis of magnetic nanoparticles and modification of polysaccharides, resulted in two articles **H9** and **A18**. In addition, Microtox® studies as a preliminary assessment of the cytotoxicity of materials with biomedical applications performed by Dr Dariusz Młynarczyk from this team were included in publications **H9**, **A14, A3, A5**. As part of the established cooperation, in 2021, Rafał Krakowiak, M.Sc., a doctoral student of Prof. Tomasz Gośliński, completed a three-

month research internship under my supervision (1.05.2021-31.07.2021) as part of the NanoBioTech Interdisciplinary Doctoral Studies project, which resulted in publications **A2** and **A4.** Thanks to the cooperation with Prof. Tomasz Gośliński, Ph.D., I have also established contact with Prof. Dr. Jadwiga Mielcarek and Dr. Jarosław Piskorz from the Department of Inorganic and Analytical Chemistry at the UMP, which led to joint papers **A18 and A8**.

Since 2018, I have also been continuously collaborating with Dr Emilia Piosik and Prof Tomasz Martyński from the Department of Materials Engineering and Technical Physics, Institute of Materials Research and Quantum Engineering, Poznań University of Technology. The research work we are carrying out together concerns the interaction of magnetic nanoparticles coated with polysaccharides, obtained by me, with a model of a biological membrane in a Langmuir-Blodgett thin film formed by appropriate phospholipids, and was part of the PRELUDIUM project funded by NCN and implemented by Dr Emilia Piosik. We are currently working on investigating the incorporation into phospholipid layers of magnetic nanoparticles coated with polysaccharides and a clinically applicable photosensitiser. Three articles have been published to date as part of the collaboration: **A16, A11, A9, and** more are in preparation.

5.2. Scientific activities carried out in cooperation with foreign centres

The use of carriers for the immobilisation of enzymes catalysing the kinetic separation of racemic active substances led to the collaboration of with Prof Ivan Vander Heyden's team at the Department of Analytical Chemistry, Applied Chemometrics and Molecular Modelling of the Vrije Universiteit Brussel. The collaborative research work involved the stereoselective esterification of racemic flurbiprofen, which was published in paper **A25**.

The publication of these results also led to the establishment of contact and effective cooperation with Prof. Gudmundur G. Haraldsson of the Science Institute University of Iceland. In paper **A13,** we published joint results of *Candida antarctica* lipase-catalysed reactions obtained for the enzyme in free form and immobilised on supports.

The nanoparticles I obtained have also been used in the '*ligand fishing*' technique. In collaboration with Prof. Ruin Moaddel of the National Institute on Aging, Bethesda, Maryland (USA), we carried out studies on the immobilisation of the androgen receptor on the surface of the materials I obtained, and the subsequent use of such an arrangement in selective ligand uptake. The results were published in publication **A21**, which is not part of the scientific achievement.

Collaboration with Dr Mariana Kozlowska of the Institute of Nanotechnology Karlsruher involved molecular dynamics simulations by Dr Kozlowska helping to elucidate the structure of my modified chitosan coating magnetic nanoparticles and differences in the efficiency of immobilisation of human blood serum proteins on its

surface. The results were published in paper **H7. The** collaboration continues today with a planned three-week visit of Dr Mariana Kozłowska to my team and my one-month stay at the Institute of Nanotechnology Karlsruher Institut für Technologie under the funds of the Toruń Centre of Excellence 'Towards Personalised Medicine'.

This year, I have also established collaborations with Prof. Tania Limongi from the Department of Applied Science and Technology Politecnico di Torino (we are planning a one-month academic exchange in 2023) and Prof. Dr. Petr Zimcik from the Department of Pharmaceutical Chemistry and Drug Analysis, Faculty of Pharmacy in Hradec Kralove, with whom we have jointly submitted a PhD project to the Academia Copernicana Interdisciplinary Doctoral School, which will be carried out by Aleksander Smolarkiewicz-Wyczachowski, M.Sc. from October this year. From 28 July to 10 August, I completed a two-week internship at the Faculty of Pharmacy in Hradec Kralove, where I gave an invited lecture as part of a faculty seminar.

6. Presentation of teaching and organizational achievements as well as achievements in the popularization of science or art

One of the basic tasks that an academic teacher must perform in accordance with the idea of a university is to educate young people and pass on their knowledge and experience. This idea has guided me throughout my academic activity to date. Working with students, alongside my academic work, is my passion. During my academic activity, I have taught a number of classes, most of which are original subjects developed independently or in collaboration. I update the content of my classes on an ongoing basis, trying to convey knowledge to students in an accessible manner. I think that my approach to teaching and my openness has contributed to the fact that since the beginning of my teaching activity I have promoted a large number of graduates: bachelor of chemistry, master of chemistry and pharmacy. I am also the assistant supervisor of doctoral students who, after obtaining their master's degrees, undertook further research work under my supervision.

My approach to research and teaching was greatly influenced by the support and guidance I received from two mentors: Prof. Marek Zaidlewicz and the Prof. Andrzej Sadlej, who shaped me not only scientifically, but showed me how to inspire passion for research work and what kind of person to be. I realise how important in taking the first steps in scientific work is the support of a mentor, in 2017 I was one of the main initiators of the establishment of the 'Study with a mentor' programme at the Faculty of Chemistry, aimed at students who achieve good academic results and at the same time want to develop their scientific passions under the guidance of staff of their choice. This gives students the opportunity to be introduced to their research work and learn all aspects of it, making it easier for them to make decisions about their future scientific work. I am currently mentoring four students, and three

graduate students who have chosen me as a mentor are developing their research passions in their PhD studies (in total, I have mentored 10 students over the four years of the programme). As I mentioned, working with students is a pleasure and gives me great satisfaction, especially when the young people working 'under my guidance' are successful. My graduates have won the titles of best Graduate and Student of the Faculty of Chemistry, competitions for the best theses and scholarships from the Minister of Science and Higher Education, the Mayor of Toruń and the Rector of the University of Nicolaus Copernicus in Toruń.

From the very beginning of my scientific work, I have participated in events and actions promoting science and the Faculty of Chemistry. Together with Dr Anna Kaczmarek-Kędziera and Dr Dariusz Kędziera, we founded the Toruń School of Computational Chemistry (TSChO, https://www.facebook.com/kurstscho/) in 2009. It was a series of courses for students, postgraduates, and academics from all over Poland wishing to skilfully apply the methods of computational chemistry to solve problems they encountered in their research work as a chemist or pharmacist. To collaborate within TSChO, we have invited befriended persons from centres centres in Poland and abroad working in specific areas of computational chemistry, to ensure that their knowledge and experience is passed on in the most competent manner possible. It should be emphasised that all organisers and lecturers conducted the classes *pro bono*. A continuation of the TSChO was the inclusion in the university-wide project co-financed by the European Union under the European Social Fund - GROWTH 'Strengthening the didactic potential of the Nicolaus Copernicus University in Toruń in mathematical and natural sciences', the task 'Further training course in the teaching and application of methods of computational chemistry', in which I acted as assistant coordinator of the task for the entire duration of the project (1.10.2010 - 31. 12. 2015). This several years of work popularising computational chemistry in the community of chemists and pharmacists resulted in the writing, together with Dr Anna Kaczmarek-Kędziera and Dr Dariusz Kędziera, of the textbook "Computational Chemistry in the Organic Laboratory" (Wydawnictwo Naukowe UMK 2014), which is used by students and didacticians in many academic centres.

Due to my research interests in medicinal chemistry, I participated in the team setting up a new major in the Faculty of Chemistry called Medicinal Chemistry. The major has been in operation since the academic year 2017/2018 for degree I and 2019/2020 for degree II. I am currently a member of the faculty's Curriculum Council, whose task is to evaluate the Medical Chemistry faculty and adapt the curriculum content to the expectations of students and employers as well as the changing state of knowledge and trends in medicinal chemistry. I also teach design classes for this major as part of the university-wide programme Universitas Copernicana Thoruniensis in Futuro II - modernisation of Nicolaus Copernicus University. I also actively participated, together with Urszula Kiełkowska, PhD, Anna Kaczmarek-Kędziera, PhD, and Magdalena Gierszewska,

PhD, in the preparation of a proposal, under the European Operational Programme Knowledge Education Development (POWER), entitled KLUCZ - the development of key competencies of science and technology students at Nicolaus Copernicus University for the needs of the economy, society and the labour market. The project was implemented jointly with the Faculty of Physics Astronomy and Applied Computer Science and the Faculty of Mathematics and Computer Science in 2015-2018.

As of 2019, together with Dr Dorota Chelminiak-Dudkiewicz, we are forming a Medical Chemistry research team within the Department of Biomedical Chemistry and Polymers (by resolution of the Faculty Council), which I head.

My activities popularising science are not limited to an academic audience. For years, I have also been trying to get schoolchildren interested in chemistry. I have given several popular science lectures for high school students, organised, together with the Student Scientific Circle of Chemists, chemical demonstrations for primary schools, and participated in the Toruń Festival of Science and Arts, acting as an expert in the so-called "Experts' Box". All these activities were also aimed at promoting the Faculty of Chemistry, in which I have participated since my doctoral studies.

6.1 List of taught activities

6.1.1. Author activities

- **Cosmetic raw materials**: a subject for students of cosmetic chemistry (laboratory 90h). Subject Coordinator. Development from scratch of the concept of the subject and exercises to be carried out by students in the 90h laboratory.

- **Elements of pharmaceutical chemistry:** a subject for students of medicinal chemistry and cosmetic chemistry (30h lecture). Course coordinator. Course concept development and lecture delivery.

- **Pharmaceutical forms**: subject for students of Medical Chemistry (lecture 10h, laboratory 30h). Course coordinator. Development from scratch of the concept of the subject (lecture + laboratory) and exercises carried out by students within 30h of laboratory.

- **Classes as part of the** *Universitas Copernicana Thoruniensis in Futuro II* **project** - *modernisation of the Nicolaus Copernicus University within the framework of the Integrated University Programme* for the Medical Chemistry major - development of a concept, preparation of a and conducting classes in the form of exercises and laboratory

- **Individual research projects** for students majoring in medicinal chemistry conducted as part of the *Universitas Copernicana Thoruniensis in Futuro II* project - *modernisation of the Nicolaus Copernicus University as part of the University's Integrated Programme*. Developing the project concept and working ~~together~~ with the student.

- **Computational Organic Chemistry: a** class for Chemistry students. Subject prepared and conducted jointly with dr Anna Kaczmarek-Kędziera and Dr. Dariusz Kędziera (45 h lecture and 45 h computer lab).

- **Molecules in medicine:** a subject for Chemistry students specialising in Biomedical Chemistry. Classes developed and prepared with Dr Anna Kaczmarek-Kędziera, (10 h lecture, 10 h computer lab)

- **Medicinal chemistry**: a subject for students of medicinal chemistry. Subject coordinator. Developing a concept, preparing and delivering a lecture (15 h). Elaborating, together with dr Anna Kaczmarek-Kędziera, the conception and laboratory exercises (60 h).

- **Teaching and using the methods of computational chemistry**: a subject for doctoral students and researchers within the WZROST project, Strengthening didactic potential of the Nicolaus Copernicus University in Toruń in mathematical and natural sciences, a project co-financed by the European Union under the European Social Fund - Human Capital Operational Programme (Priority IV: Higher education and science, Measure 4.1: Strengthening and development of didactic potential of universities and increasing the number of graduates in fields of key importance for the knowledge-based economy, Sub-measure 4.1.1: Strengthening the didactic potential of universities. Subject prepared and conducted jointly with Dr hab. Anna Kaczmarek-Kędziera and Dr Dariusz Kędziera.

6.1.2. Other teaching activities

- **Personal care cosmetics**: classes for the cosmetic chemistry course. Exercises (15h).

- **Chemistry of polymers**: classes for the cosmetic chemistry course. Laboratory (30h).
- **Organic chemistry**: coursework for Biology students of the Faculty of Biology and Veterinary Sciences. Laboratory (30h).

- **Organic chemistry**: coursework for Biotechnology students of the Faculty of Biology and Veterinary Sciences. Laboratory (45h).

- **General and organic chemistry**: coursework for Biotechnology students of the Faculty of Biology and Veterinary Sciences. Laboratory (60h).

- **General and analytical chemistry**: coursework for Biotechnology students of the Faculty of Biology and Veterinary Sciences. Laboratory (40h).

- **General and analytical chemistry**: coursework for Biology students of the Faculty of Biology and Veterinary Sciences. Laboratory (40h).

- **Fundamentals of photochemistry: a** class for Chemistry majors. Laboratory (60h)

- **Cosmetic formulation: a** class for cosmetic chemistry majors. Laboratory

6.2 Textbooks and teaching materials developed

- Anna Kaczmarek-Kedziera, Dariusz Kedziera, **Marta Ziegler-Borowska**, Computational chemistry in the organic laboratory, ISBN 977-83-231-3114-4, Wydawnictwo Naukowe Uniwersytetu Mikołaja Kopernika, Toruń 2014.

- **Marta Ziegler-Borowska**, Andrzej Wolan, Drug synthesis and pharmaceutical form, English-language materials for the author's course within the KATAMARAN project (PPI/KAT/2019/1/00018/U/00001) funded by the National Agency for Academic Exchange NAWA for 2019-2021.

- Development of electronic materials for the supplementary course in the field of teaching and applying computational chemistry methods within the framework of the WZROST UMK project - Strengthening didactic potential of the Nicolaus Copernicus University in Toruń in mathematical and natural sciences, a project co-financed by the European Union under the European Social Fund - Human Capital Operational Programme (Priority IV: Higher education and science, Measure 4.1: Strengthening and development of didactic potential of universities and increasing the number of graduates in fields of key importance for the knowledge-based economy, Sub-measure 4.1.1: Strengthening the didactic potential of universities. Years 2010-2015.

- Development of teaching materials for participants in the "Toruń School of Computational Chemistry"

- Preparation and development of teaching materials for students for all my original courses in Chemistry, Cosmetic Chemistry and Medicinal Chemistry: 8 subjects in total.

6.3 Academic supervision of students

A total of **17 master's theses**, **25 bachelor's theses were** produced under my supervision after the doctoral degree between 2012 and 2022. I reviewed **15 diploma theses**. I acted as an assistant supervisor in the doctoral thesis of Dr Dorota Chełminiak-Dudkiewicz defended in 2017 (supervisor Prof. Dr. Halina Kaczmarek). At present, I am the assistant supervisor of **5 doctoral students:** two PhD students - Katarzyna Węgrzynowska-Drzymalska MA (supervisor prof. dr hab. Halina Kaczmarek) and Kinga Mylkie MA (supervisor prof. dr hab. Andrzej Wojtczak), PhD student Paweł Nowak MA (supervisor prof. dr hab. Halina Kaczmarek), implementation doctoral student Piotr Maćczak (supervisor Prof. dr hab. Halina Kaczmarek) and a doctoral student within the Interdisciplinary Doctoral School Academia Copernicana, Aleksander Smolarkiewicz-Wyczachowski (together with Prof. dr hab. Petr Zimcik). On several occasions I have acted as a mentor for first year students in Chemistry and Medicinal Chemistry. In addition, I have acted as a mentor within the "Study mentor programme for ten students and I have mentored national and international trainees.and foreign interns.

6.3.1. Master's thesis supervisor

Academic year 2021/2022

- Paweł Nowak " *Synthesis of hydrazidomethyl starch with embedded doxorubicin for selective anticancer therapy* "
- Aleksander Smolarkiewicz-Wyczachowski " *Preparation of chitosan-based composites with BODIPY dyes as potential drug forms in photodynamic therapy (PDT)* "

Academic year 2020/2021

- Agata Fornal "*Effects of micro- and nanoplastics on collagen".*
- Natalia Muczeńska "*Synthesis of chitosan composites with St. John's wort extract as potential hybrid materials for PDT therapy*".
- Agata Mikulska "*Synthesis of new materials based on chitosan modified with triazole grouping with potential antimicrobial activity*".

Academic year 2019/2020

- Patrycja Grębicka "*Interaction of microplastics isolated from cosmetic products with serum albumins*".

Academic year 2018/2019

- Patryk Rybczynski "*Photostability study of 4,4-difluoro-8-(4-(3-aminopropoxy)phenyl)-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene,4,4-difluoro-8-*

(4-(3-(1,3-dioxoisoindolin-2-yl)propoxy)-phenyl)-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene and their iodinated derivatives"

- Kinga Mylkie '*Effect of oxidative stress on the binding of ketoprofen by human serum albumin immobilised on magnetic nanoparticles coated with aminated starch*' (thesis awarded in the best thesis competition).

Academic year 2016/2017

- Paweł Wesołowski "*Synthesis and characterisation of chitosan enriched in aldehyde groups*".
- Magdalena Mankowska "*Study of the photostability of chitosan membranes with the addition of porphyrin complexes*".
- Daria Kosmalska "*Synthesis and photostability of dialdehyde pectin as a new crosslinking agent for polymer coatings*".

Academic year 2016/2017

- Agata Michalska "*Synthesis and UV photostability study of dialdehyde starches with different contents of carbonyl groups*".

Academic year 2014/2015

- Ewelina Stasiak "*Synthesis and stability study of modified chitosan for biomedical applications*"

Academic year 2012/2013

- Piotr Maćczak "*Photochemical and physical properties of 2,4-bis[(amino)phenyl]cyclobutane-1,3-diol and their mixtures with chitosan"*.
- Dorota Chełminiak-Dudkiewicz (Chełminiak) "*Synthesis and application of magnetite nanoparticles stabilised with modified chitosan for immobilisation of lipases*" (thesis awarded in the competition for the best thesis)

Academic year 2011/2012

- Sebastian Dwojak "*Synthesis of triżelazium tetroxide nanoparticles for immobilisation of lipases*".
- Anna Bieganowska "*Synthesis and properties of new polystyrene materials modified with 3-phenyl-2-methylpropanal hydantoin system*".

6.3.2. Bachelor thesis supervisor

Academic year 2020/2021

- Magdalena Rutkowska " *Influence of pH on the structure of the resulting BSA and HSA nanocrystals*"
- Monika Mytlewska " *Synthesis of chitosan with hydrazine grouping as a material for selective drug delivery*"

Academic year 2020/2021

- Oktawia Kalisz "*Pellets as a multi-reservoir drug form - manufacturing methods and characteristics*
  production methods and characteristics"
- Michalina Pożarowska "*Protein nano-flowers for medical applications*".

Academic year 2019/2020

- Jakub Gauza "*Synthesis and properties of saccharine compounds with heterocyclic system for biomedical applications*".
- Aleksander Smolarkiewicz-Wyczachowski "*Study of the photochemical properties of new BODIPY-type compounds*".
- Paweł Nowak "*Investigation of the interaction of propranol with α1-acid glycoprotein by spectroscopic methods*".

Academic year 2018/2019

- Paula Pocheć " *Evaluation of the photostability of zinc and ferrous phthalocyanine as clinically used drugs in PDT*"
- Agata Fornal (Serowka) "*Interaction of magnetic nanoparticles coated with chitosan and bovine serum albumin with ketoprofen*".
- Agata Mikulska "*Study of the effect of oxidative stress on the degree of ketoprofen binding by the free form of HSA and BSA*"
- Karolina Sandach "*Study of the interaction of bovine serum albumin with ketoprofen using SPR - surface plasmon resonance technique*".

Academic year 2017/2018

- Patrycja Grębicka "*Synthesis of microcrystalline polysaccharides: pectin and cellulose coated with titanium dioxide for potential cosmetic applications*".

Academic year 2016/2017

- Justyna Palińska "*Preparation and study of the effect on skin hydration level of a moisturising mask with magnetic nanoparticles*".
- Alicja Zielińska "*Study of the potential use of magnetic nanoparticles coated with chitosan and amphiphilic polymer as sorbents for ketoprofen*".
- Patryk Rybczynski "*Investigation of the use of carbonaceous materials as potential sorbents for ketoprofen in aqueous environments*".
- Kinga Mylkie "*Immobilization of bovine serum albumin on chitosan-coated magnetite nanoparticles*".

Academic year 2015/2016

- Łukasz Marecki "*Preparation of chitosan membranes with betulin isolated from birch bark*".

- Emil Grodzicki "*Photopolymerisation of an oleogel based on poly(acrylic acid) enriched with silver nanoparticles*".
- Damian Podgródny "*Development of a method for the preparation of poly(acrylic acid)-coated sensors for SPR technology*".
- Oliwia Tybinska "*Synthesis of chitosan microcapsules with green tea extract for cosmetic applications*".

Academic year 2014/2015

- Marta Kiżewska "*Cosmetic use of raw materials extracted from cocoa beans*".

Academic year 2013/2014

- Joanna Wierzchowska "*Application of compounds from the quinone group in cosmetic products*".
- Aleksandra Andrzejczyk "*The use of plants from the Asteraceae family in cosmetics*".
- Joanna Gliszczyńska "*Squarine dyes - methods of production and applications*".
- Paulina Gołębiewska "*Biomedical and catalytic applications of magnetic particles*".

6.4 Supervising doctoral students as a supervisor or assistant supervisor

Mentoring as an assistant supervisor

- Dr Dorota Chełminiak-Dudkiewicz '*Structure and properties of novel polymer-coated magnetic nanoparticles as potential supports in catalysis*'. Doctoral thesis defended with distinction on 28.04. 2017. (main supervisor Prof. Dr. Halina Kaczmarek)
- Katarzyna Węgrzynowska-Drzymalska MA (supervisor Prof. Dr. Halina Kaczmarek)
- Mgr Piotr Maćczak (implementation doctorate, supervisor Prof. Dr. Halina Kaczmarek)
- MA Kinga Mylkie (supervisor Prof. Dr. Andrzej Wojtczak)
- MA Paweł Nowak (supervisor Prof. Halina Kaczmarek)
- Aleksander Smolarkiewicz-Wyczachowski, M.A. (supervisor Prof. Dr. Petr Zimcik)

6.5 Scientific supervision of national and international trainees

- **Gwenn Tani, Faculty of** Process and Bioprocess Engineering, Polytech Nantes-Saint Nazaire, France. Pre-doctoral. Internship as part of the Erasmus plus programme, 23.05.2022-23.08.2022.

- **Matthieu Rouger,** Faculty of Process and Bioprocess Engineering, Polytech Nantes-Saint Nazaire, France. Pre-doctoral. Internship as part of the Erasmus plus programme, 23.05.2022-23.08.2022.

- **Giorgia Crescitelli**, Faculty of Biotechnology, Foggia University, Italy. Internship
  as part of the Erasmus plus programme, 27.02.2022 - 17.06.2022.

- **Rafał Krakowiak, M.Sc.,** Chair and Department of Chemical Technology of Medicinal Products at the Karol Marcinkowski University of Medical Sciences in Poznań, Ph.D. student (pre-doctoral), internship within the NanoBioTech Interdisciplinary Doctoral Studies project 1.05.2021-31.07.2021.

- **Maëlann Le Paih-Danet**, Faculty of Process and Bioprocess Engineering, Polytech Nantes-Saint Nazaire, France. Pre-doctoral. Internship as part of the Erasmus plus programme, 24.05.2021-23.08.2021.

- **Dr Edyta Stefaniszyn**, Department of Organic Chemistry, Faculty of Pharmacy, Medical University of Lublin. One-month research internship (March 2016).

6.6 Science dissemination and organisational activities

From 2017 to 2020, I served as the chairperson of the "Young People's Council" appointed by the Dean of the Faculty of Chemistry Prof. Dr. Edward Szłyk to work for the promotion of the Faculty of Chemistry and popularisation of science. Currently, since 2020, I am a member of the new Team for the Promotion and Popularisation of Science and the Programme Council of the Medical Chemistry faculty. Every year I actively participate in in organising and conducting the "Open Doors of the Faculty of Chemistry at the University of Nicolaus Copernicus University". I have actively participated in the work of teams preparing grant applications within the POWER programme (NCBiR), the European Social Fund - Human Capital Operational Programme (Priority IV: Higher Education and Science) and creating the faculty of Medical Chemistry at the S1 and S2 degree. Between 2010 and 2015, I acted as assistant coordinator of the task "Further training course in teaching and application of computational chemistry methods" within the project from the European Social Fund - GROWTH 'Strengthening the teaching potential of the Nicolaus Copernicus University in Toruń in mathematical and natural sciences'. My activities have twice been recognised in the form of the UMK Rector's team award for organisational achievements (2017 and 2021).

- **Cooperation with the Foundation Amicus UMK**

Participation in science festivals, expert duty in the UMK tent (Toruń Days), conducting a two-hour workshop for parents as part of the UMK Children's University, participation in the 'Experts' Lodge' of the Graduate Programme, participation in the Science and Art Festival Festival of Science and Arts.

- **Cooperation with Primary Schools and High Schools**

Preparing and carrying out workshops for pupils at Primary School No 27 in Toruń as part of the 'Be like Ignacy' educational programme. Preparing and conducting popular science lectures for primary and secondary school students as part of workshops organised at the Department of Chemistry. Preparing and conducting classes in the form of a pre-matriculation course "Last Bell" organised at the Faculty of Chemistry of the Nicolaus Copernicus University. Assistance in the organisation of the 2022 baccalaureate test under the auspices of the Faculty of Chemistry at the Nicolaus Copernicus University.

- **Work on behalf of the Faculty of Chemistry at the Nicolaus Copernicus University**

2020-present
Member of the Team for Promotion and Popularisation of Science at the Faculty of Chemistry, UMK, appointed by the Dean of the Faculty of Chemistry, Prof. Dr. Iwona Łakomska.

2020-present
Representative of assistant professors on the Discipline Council of the Faculty of Chemistry of the University of York.

2021-present
Member of the Programme Board of the Medical Chemistry course at the Faculty of Chemistry, UMK.

2017-2020
Chairperson of the "Youth Council" appointed by the Dean of the Faculty of Chemistry, Prof. Dr. Edward Szłyk, to promote the Faculty of Chemistry of the University of Nicolaus Copernicus.

2016-2020
Representative of assistant professors on the Council of the Faculty of Chemistry of the University of York.

2017
Working as part of a team preparing the creation of a new course at the Faculty of Chemistry of the University of Nicolaus Copernicus University: Medical Chemistry in the second degree.

2016
Team preparation of an application under the European Operational Programme Knowledge Education Development (POWER), entitled KRYPTON - Competent graduate on the labour market - a competence development programme for students of the Faculty of Chemistry at UMK in TOruN. Funding was awarded for 2016-2019. The Faculty abandoned the project due to insufficient numbers of students.

2016
Working as part of a team preparing the creation of a new course at the Faculty of Chemistry of the University of Nicolaus Copernicus University: Medicinal Chemistry in first degree studies.

2015
Team preparation of a proposal under the European Operational Programme Knowledge Education Development (POWER), entitled KLUCZ - development of key competencies of science and technology students at Nicolaus Copernicus University for the needs of the economy, society and the labour market. The project received funding for 2015-2018.

2010-2015
Assistant task coordinator in the WZROST project 'Strengthening the teaching potential of the Nicolaus Copernicus University in Toruń in mathematical and natural sciences' task 'Further training course in teaching and applying methods of computational chemistry'.

2010
Working in a team preparing an application under the European Social Fund - GROWTH "Strengthening the teaching potential of the Nicolaus Copernicus University in Toruń in mathematical and natural sciences' task 'Further training course in the field of teaching and applying computational chemistry methods'. The project received funding for 2010-2015.

7. Apart from information set out in 1-6 above, the applicant may include other information about his/her professional career, which he/she deems important

7.1 Research activities before the PhD degree

In the year 2000, I completed my Bachelor's studies at the Faculty of Chemistry at the Nicolaus Copernicus University with a very good result, defending my Bachelor's thesis "*Synthesis and use of benzene, toluene and xylenes*" written under the supervision of Prof. Dr. Marek Zaidlewicz. I continued my studies with a supplementary master's degree in chemistry from October of the same year. My master's thesis, like my bachelor's thesis, was carried out in the Department of Organic Chemistry, this time under the supervision of Dr Adam Dzieleńdziak. The topic of my thesis was the synthesis of a new, undescribed in the literature boronated amino acid, which could find application in the innovative anticancer therapy BNCT (*Boron Neutron Capture Therapy*). Developing the synthesis of this compound from scratch required me to learn a number of methods of modern organic synthesis and to learn how to work with organometallic compounds. My master's thesis entitled. I defended my thesis entitled "*Synthesis of methyl-p-dihydroxyborylphenylalanine*" in June 2002, obtaining a very good grade and, at the same time, the title of "Best graduate of the Faculty of Chemistry at the Nicolaus Copernicus University".

Due to my scientific interest in anticancer drugs, I decided to continue my work and develop my skills under the supervision of Prof. Marek Zaidlewicz in the field of BNCT by commencing my PhD studies at the Faculty of Chemistry, UMK, in October 2002. From the very beginning, my research was part of a grant under the supervision of Prof. Marek Zaidlewicz entitled "*Low molecular weight boron carriers for BNCT therapy*". The topic of my PhD thesis was the synthesis of boronated amino acid analogues of BPA (p-dihydroxyborylphenylalanine), a drug clinically used in BNCT therapy in glioma patients. I have developed, carried out and optimised the synthesis of four BPA analogues. Each of the compounds, was a new hitherto unpublished boronated amino acid whose synthesis involved a minimum of six steps. While carrying out my research work under the supervision of Prof. Marek Zaidlewicz, I became familiar with methods of advanced organic synthesis and learnt how to handle problems that can be encountered in multi-stage synthesis. While trying to deeply understand the mechanisms guiding my reactions and encountering difficulties along the path of synthesis, I simultaneously developed my interest in computational chemistry under the guidance of the late Prof. Andrzej Sadlej. Working under the guidance of both professors taught me a "broader view" of research topics, the ability to deal with research problems and to work in an interdisciplinary team.

In 2005, I was awarded the "INNOREG - European Scholarship for Doctoral Students - Innovation for the Region" grant for the best doctoral students in the Kujawsko-Pomorskie Voivodship. Thanks to the funding, I was able to go for a one-week stay at the Research Centre in Studsvik, Sweden,with which I established cooperation (Prof. Jacek Capała, PhD), and which was the only radiotherapy clinic in Europe conducting clinical research on BNCT.

Some of the results I obtained in my research were published in **A1.** (Marek Zaidlewicz*, Joanna Cytarska, Adam Dzielendziak, **Marta Ziegler-Borowska**, Synthesis of boronated phenylalanine analogues with a quaternary centre for boron neutron capture therapy. *Arkivoc*, **2004**, 3, 11-27), and others were presented at national and international conferences.

My activities outside of my scientific work also consisted of several teaching activities: laboratory and organic chemistry exercises and supervising MSc students.

During my doctoral studies in 2005, I was offered a position as an assistant in the Department of Organic Chemistry of the Faculty of Pharmacy at the L. Rydygier Medical College of the Nicolaus Copernicus University in Bydgoszcz. In March 2006, when it seemed that my PhD research work was nearing completion with the consent of Prof. Marek Zaidlewicz, I decided to take up this full-time position at the KiZ. Organic Chemistry at the Faculty of Pharmacy, CM UMK, under the supervision of Prof. Dr. Bożena Modzelewska-Banachiewicz, while continuing the synthesis of the last of the BPA analogues planned as part of my doctoral thesis.

As the Department of Organic Chemistry at the Faculty of Pharmacy was a newly established unit, working on a full-time basis required me to prepare many new teaching activities, as well as organisational activities involving the purchase of equipment and furnishing the Department's premises in the new Faculty of Pharmacy building. I also undertook research topics related to the related to the activity of Prof. Modzelewska-Banachiewicz, consisting in the synthesis and characterisation of triazole compounds with potential antimicrobial activity. The obtained results were published in a publication **A 33** sent to a journal before the defence of the PhD thesis.

Between 2007 and 2010, due to my son's serious illness, I had to withdraw somewhat from scientific activity, but I managed to finalise my PhD thesis, which I defended in December 2009 before the Council of the Faculty of Chemistry of the University of Bremen. Due to my son's difficult health situation, I also had to cancel a planned trip to Jacobs University Bremen for a one-year postdoctoral fellowship under Prof. Dr. Detlef Gabel.

7.2 Research activities after awarded PhD

I obtained my PhD in chemistry in December 2009. In February 2010, based on an agreement between the parties, I was employed as an assistant in the Department of Chemistry and Photochemistry of Polymers at the Faculty of Chemistry of the Nicolaus Copernicus University in Toruń, headed by Prof. Halina Kaczmarek, Ph.

Being employed in a team working on the photochemistry and characterisation of polymeric materials required me to take a new look at my research topics. Having a background in the organic synthesis of active substances, I decided to focus on the modification and synthesis of new polymeric materials. At the same time, I was completing several projects that I had started while still working at the Faculty of Pharmacy. The first published papers **A30-A32** concerned the synthesis of fluorescent organic compounds (**A32**) and the characterisation of polymeric materials with photosensitive and bactericidal compounds (**A30-A31**). Working on these projects exposed me to the methodology of polymeric materials research and the fundamentals of photochemistry, which was a complete change of subject matter for a synthesist. However, my research interests continued to focus on medicinal chemistry and medicinal chemistry, so I decided to find a topic that would allow me to combine them with polymer chemistry and photochemistry. When reviewing the scientific literature, articles describing biomedical applications of magnetic nanoparticles (MNPs) particularly caught my attention. Since the synthesis of a magnetic core was not complicated and its surface could be modified with both small- and large-molecule compounds, I decided to try the synthesis of magnetic nanoparticles coated with a polymeric material. The first nanoparticles I obtained were coated with pure, unmodified chitosan. I cross-linked the polymer coating with epichlorohydrin. At the same time, my former MSc student, now dr n. far. Tomasz Siódmiak, started work under the supervision of Prof. Michał Marszałł on the use of lipases for kinetic separation of NSAID drugs. We decided to use nanoparticles obtained by me to immobilise the enzyme and kinetically separate racemic ibuprofen. After a successful attempt to synthesise MNPs and immobilise proteins on their surface, I decided to continue my research work in this area. I presented my scientific plans concerning the synthesis of polysaccharide-modified magnetic nanoparticles for biomedical applications in detail in March 2012 at a promotion seminar in the presence of faculty members and the Dean for Science, Prof. Andrzej Wojtczak, PhD. After the authorities of the faculty gave a positive opinion on the presented scientific plans, I was employed as an assistant professor in October of the same year. From that moment on, I started carrying out research towards my habilitation. The first publication containing results on the synthesis and characterisation of MNPs obtained by me coated with chitosan and the amphiphilic polymer was published in 2013 (**A30**). Subsequent papers were published 2013-2020 and concerned the synthesis and characterisation of new nanoparticles containing reactive functional groups on the surface, not yet described

in the literature, and were included in a series of publications constituting a scientific achievement (**H1-H9**). The materials I obtained have been successfully used as effective supports in catalytic reactions and the results obtained have been published in publications **A25-A27**, **A23**, **A19-A21**, which are not included in the series of publications constituting the scientific achievement. In addition to the synthesis of magnetic nanoparticles, I have completed the synthesis of a boronic acid containing system 2-tetralone system, which is the subject of the obtained patent **PL No 215215**, and I worked on the synthesis of new monomers and polymeric materials (the results were published in publications **A28 - A30** and are the basis for the granted patent **PL No 215809**).

As one of the lines of research conducted in the Department of Chemistry and Photochemistry of Polymers was the determination of the effect of radiation on polymer materials and their composites, due to my experience in organic synthesis, I also took up the continuation of this topic. In 2013, I became the main contractor in the project 'Research on the potential use of saccharine dyes in modern materials chemistry' carried out under the Iuventus Plus grant of the Ministry of Science and Higher Education**,** headed by Dr Anna Kaczmarek-Kędziera.

In 2014, together with Dr Anna Kaczmarek-Kędziera, we prepared and submitted a grant application in the OPUS 7 competition (NCN, 2014/13/B/ST8/04342) entitled. "Design and synthesis of porous materials based on biopolymers and their composites with magnetite as potential sorbents for NSAID drugs", which received funding (grant manager Dr hab. Anna Kaczmarek-Kędziera), in which I acted as principal investigator. The proposal was largely based on the synthesis of magnetic nanoparticles designed by me and their subsequent use in the synthesis of magnetic carbon materials. In the same year, I prepared and applied to the NCN SONATA 8 competition "Synthesis and study of the interaction of magnetic nanoparticles coated with human serum protein with selected drugs under normal and artificially induced oxidative stress conditions", which received funding (2014/15/D/NZ7/01805, headed by Dr M. Ziegler-Borowska). A year later, together with Prof. Dr. Michał Marszałł, we received funding for another OPUS 8 project (2014/15/B/NZ7/00972) "Synthesis, characterisation and activity evaluation of biopolymer-modified magnetic nanoparticles as potential enzyme carriers in the synthesis of beta-blocker drugs". This resulted in my focus in 2014-2019 on the design and synthesis of new polymeric materials and coated magnetic nanoparticles. The papers published during this period are related to these topics and are part of the series of publications constituting the scientific achievement (**H3-H8**). In addition, Dr Dorota Chełminiak-Dudkiewicz, within the framework of her PhD thesis, of which I was the associate supervisor, investigated the usefulness of materials obtained by me as lipase carriers in catalytic reactions (**A19-A23**, **A26-A27**). The nanoparticles I obtained were also used in studies of their ability to interact with a model biological membrane - a thin phospholipid layer, by the team of Dr. Emilia Piosik from the Poznań University of

Technology. The results of these studies have been published in papers **A16**, **A11** and **A9**.

The synthesis of new magnetic nanoparticles required, as I have already mentioned, the design and preparation of functional polymeric materials. In my research, I decided to use only natural polymers in particular polysaccharides. The experience I gained allowed me to start research on finding new, non-toxic, and effective crosslinking agents for polysaccharides and proteins (**A14**, **A24**) and also to undertake an assessment of the photochemical stability of the polymeric coatings used (**A6**, **A17**). The polymeric materials obtained have also found application as novel flocculants for water purification (**A7**).

During my scientific work I have also collaborated with the economic environment (Ekomer, Synthex Technologies, Sorimex). I consider the most scientifically fruitful cooperation to be with Sorimex, a company that manufactures Class I medical devices such as ECG electrodes and conductive gels. As part of the collaboration, I led work on improving the performance properties of the photo-curable gel used in electrode manufacture. The results obtained allowed me to write a research agenda with the company as part of the Regional Operational Programme of the Kuyavian-Pomeranian Voivodeship 2014-2020 - ERDF as well as to establish a research and development centre in the company to increase the company's innovativeness (project number: RPKP.01.02.01-04-0033/17). The cooperation continues to this day, and the company was ranked first in the Kujawsko-Pomorskie Voivodeship in the Forbes Monthly Diamonds 2022 poll.

My scientific work has been recognised by H.M. Rector of the University of Nicolaus Copernicus in the form of awards received (4 awards) and team honours for scientific activities (3 awards) and scholarships for high-scoring publications (11 scholarships). In 2019, I received a nomination for the Polish Intelligent Development Award for my project funded by the SONATA 8 grant "Synthesis and study of the interaction of magnetic nanoparticles coated with human blood serum protein with selected drugs under normal and artificially induced oxidative stress conditions".

7.2.1. Publications related to other research achievements

A2. Rafał Krakowiak, Robert Frankowski, Kinga Mylkie, Michał Kotkowiak, Dariusz T. Młynarczyk, Alina Dudkowiak, Beata Jadwiga Stanisz, Agnieszka Zgoła-Grześkowiak, **Marta Ziegler-Borowska**, Tomasz Gośliński*, Titanium(IV) oxide nanoparticles functionalized with variousmeso-porphyrins for efficient photocatalytic degradation of ibuprofen in UV and visible light, *J. Environ. Chem. Eng.* ,**2022**, 10 (5),1-17, DOI:10.1016/j.jece.2022.108432,
IF$_{2021}$ 7.968 ; MNiSW points 100, Q1

A3. Katarzyna Węgrzynowska-Drzymalska, Dariusz T. Młynarczyk, Dorota Chełminiak-Dudkiewicz, Halina Kaczmarek, Tomasz Gośliński, **Marta Ziegler-Borowska**, Chitosan-gelatin films cross-linked with dialdehyde cellulose

nanocrystals as potential materials for wound dressings, Int. J. Mol. Sci., **2022**, 23 (17), 1-28, DOI:10.3390/ijms23179700,
IF$_{2021}$ 6,208; MNiSW points 140, Q1

A4. Paweł Bakun, Beata Czarczyńska-Goślińska, Dariusz T. Młynarczyk, Marika Musielak, Kinga Mylkie, Jolanta Długaszewska, Tomasz Koczorowski, Wiktoria M. Suchorska, **Marta Ziegler-Borowska**, Tomasz Gośliński*, Gallic acid-functionalized, TiO2-based nanomaterial : preparation, physicochemical and biological properties, *Materials*, **2022,** 15(12,) , pp. 1-19,doi:10.3390/ma15124177,
IF$_{2021}$ 3.748; MNiSW points 140, Q2

A5. Katarzyna Wegrzynowska-Drzymalska, Kinga Mylkie, Pawel Nowak, Dariusz T. Mlynarczyk, Dorota Chelminiak-Dudkiewicz, Halina Kaczmarek, Tomasz Goslinski, **Marta Ziegler-Borowska***, Dialdehyde Starch Nanocrystals as a Novel Cross-Linker for Biomaterials Able to Interact with Human Serum Proteins. *Int. J. Mol. Sci*., **2022**; 23(14), 7652. doi:10.3390/ijms23147652
IF$_{2021}$ 6,208; MNiSW points 140, Q1

A6. Dorota Chelminiak-Dudkiewicz*, Aleksander Smolarkiewicz-Wyczachowski, Katarzyna Wegrzynowska-Drzymalska, **Marta Ziegler-Borowska***, Effect of Irradiation on Structural Changes of Levan. *Int. J. Mol. Sci*., **2022,** 23(5), 2463 doi: 10.3390/ijms23052463
IF$_{2021}$ 6,208; MNiSW points 140, Q1

A7. Piotr Maćczak*, Halina Kaczmarek*, **Marta Ziegler-Borowska,** Katarzyna Węgrzynowska-Drzymalska, Aleksandra Burkowska-But, The Use of Chitosan and Starch-Based Flocculants for Filter Backwash Water Treatment. *Materials* (Basel), **2022**, 15, 1056 doi: 10.3390/ma15031056
IF$_{2021}$ 3.748; MNiSW points 140, Q2

A8. Patryk Rybczyński, Aleksander Smolarkiewicz-Wyczachowski, Jarosław Piskorz, Szymon Bocian, **Marta Ziegler-Borowska**, Dariusz Kędziera, Anna Kaczmarek-Kędziera *, Photochemical properties and stability of BODIPY dyes. *Int. J. Mol. Sci*., **2021**, 22 (13), 6735 doi: 0.3390/ijms22136735
IF$_{2021}$ 6,208; MNiSW points 140, Q1

A9. Emilia Piosik *, Aleksandra Zaryczniak, Kinga Mylkie, **Marta Ziegler-Borowska*,** Probing of interactions of magnetite nanoparticles coated with native and aminated starch with a DPPC model membrane. *Int. J. Mol. Sci*., **2021**, 22 (11), 5939 doi:10.3390/ijms22115939
IF$_{2021}$ 6,208; MNiSW points 140, Q1

A10. Halina Kaczmarek *, Patryk Rybczyński, Piotr Maćczak, Aleksander Smolarkiewicz-Wyczachowski, **Marta Ziegler-Borowska,** Chitosan as a Protective Matrix for the Squaraine Dye. *Materials* (Basel), **2021,** 14(5), 1171, doi:10.3390/ma14051171
IF$_{2021}$ 3.748; MNiSW points 140, Q2

A11. Emilia Piosik *, **Marta Ziegler-Borowska *,** Dorota Chełminiak-Dudkiewicz, Tomasz Martyński, Effect of aminated chitosan-coated Fe3O4 nanoparticles with applicational potential in nanomedicine on DPPG, DSPC, and POPC Langmuir monolayers as cell membrane models. *Int. J. Mol. Sci*., **2021,** 22(5), 2467, doi:10.3390/ijms22052467
IF$_{2021}$ 6,208;, MNiSW points 140, Q1

A12. Kinga Mylkie, Paweł Nowak, Patryk Rybczyński, **Marta Ziegler-Borowska** *. Polymer-Coated Magnetite Nanoparticles for Protein Immobilization. *Materials* (Basel), **2021**, 14(2), 248; doi: 10.3390/ma14020248
IF$_{2021}$ 3.748; MNiSW points 140, Q2

A13. Tomasz Siódmiak *, Gudmundur G. Haraldsson, Jacek Dulęba, **Marta Ziegler-Borowska,** Joanna Siódmiak, Michał P.Marszałł, Evaluation of designed immobilized catalytic systems : activity enhancement of lipase B from Candida antarctica. *Catalysts*, **2020**, *10*, doi: 10.3390/catal10080876
IF$_{2020}$ 4.146 , IF$_{2021}$ 4.501; MNiSW points 100, Q2

A.14. Katarzyna Węgrzynowska-Drzymalska, Patrycja Grębicka, Dariusz T. Młynarczyk, Dorota Chełminiak-Dudkiewicz, Halina Kaczmarek, Tomasz Gośliński, **Marta Ziegler-Borowska *,** Crosslinking of chitosan with dialdehyde chitosan as a new approach for biomedical applications. *Materials* (Basel), **2020**,*13*, doi: 10.3390/ma13153413
IF$_{2020}$ 3.623, IF$_{2021}$ 3.748; MNiSW points 140, Q2

A.15. Piotr Maćczak, Halina Kaczmarek *, **Marta Ziegler-Borowska**, Recent achievements in polymer bio-based flocculants for water treatment. *Materials* (Basel),**2020,** 13, doi: 10.3390/ma13183951
IF$_{2020}$ 3.623, IF$_{2021}$ 3.748; MNiSW points 140, Q2

A16. Emilia Piosik*, Paweł Klimczak, **Marta Ziegler-Borowska,** Dorota Chełminiak-Dudkiewicz, Tomasz Martyński, A detailed investigation on interactions between magnetite nanoparticles functionalized with aminated chitosan and a cell model membrane. *Mat. Sci. Eng*.: *C*, **2020**, *109*, 110616; doi: 10.1016/j.msec.2019.110616
IF$_{2020}$ 7.328, IF$_{2021}$ 8.457; MNiSW points 140, Q1

A17. Marta Ziegler-Borowska*, Katarzyna Wegrzynowska-Drzymalska, Dorota Chelminiak-Dudkiewicz, Jolanta Kowalonek, Halina Kaczmarek. Photochemical Reactions in Dialdehyde Starch,. *Molecules*, **2018**, *23*, 3358; doi: 10.3390/molecules23123358
IF2018 3,060 ; IF2021 4,927; MNiSW points 140, Q2

A18. Dorota Chełminiak-Dudkiewicz**, Marta Ziegler-Borowska,** Magdalena Stolarska, Lukasz Sobotta, Michal Falkowski, Jadwiga Mielcarek, Tomasz Goslinski, Jolanta Kowalonek, Katarzyna Węgrzynowska-Drzymalska, Halina Kaczmarek*. The chitosan-Porphyrazine hybrid materials and their photochemical properties. *J. Photochem. Photobiol. B: Biology*, **2018**, *181*, 1-13; doi: 10.1016/j.jphotobiol.2018.02.021
IF2018 4,067 ; IF2021 6,814; MNiSW points 100, Q1

A19. Adam Sikora, Dorota Chełminiak-Dudkiewicz, **Marta Ziegler-Borowska**, Michał Piotr Marszałł*. Enantioseparation of (RS)-atenolol with the use of lipases immobilized onto new-synthesized magnetic nanoparticles. *Tetrahedron Assym*., **2017**, *28*, 374-380; doi: 10.1016/j.tetasy.2017.01.012
IF2017 2.126 ; IF2021 2.126, Q2

A20. Adam Sikora, Dorota Chełminiak-Dudkiewicz, Tomasz Siódmiak, Agata Tarczykowska, Wiktor Dariusz Sroka, **Marta Ziegler-Borowska**, Michał Piotr Marszałł*. Enantioselective acetylation of (R, S)-atenolol: The use of Candida rugosa lipases immobilized onto magnetic chitosan nanoparticles in enzyme-catalyzed biotransformation. *J. Mol. Cat. B: Enzymatic*, **2017**, *134*, 43-50; doi: 10.1016/j.molcatb.2016.09.017
IF2017 2,269 ; IF2021 2,269; MNiSW points 70, Q2

A21. Michał P. Marszałł*, Wiktor D. Sroka, Adam Sikora, Dorota Chełminiak**, Marta Ziegler-Borowska,** Tomasz Siódmiak, Ruin Moaddel. Ligand fishing using new chitosan-based functionalized Androgen Receptor magnetic particles. *J. Pharm. Biomed. Anal.* , **2016**, *127*, 129-135; doi: 10.1016/j.jpba.2016.04.013
IF2017 3.255 ; IF2021 3.571; MNiSW points 100, Q2

A22. Anna Kaczmarek-Kędziera*, **Marta Ziegler-Borowska,** Dorota Chełminiak, Przemysław Kuchnicki, Halina Kaczmarek. Effect of UV-irradiation on spectral properties of squaraine dye in diluted solutions. *J. Photochem. Photobiol. A:Chemistry*,**2016**, 318, 77-89; doi: 10.1016/j.jphotochem.2015.11.011
IF2010 2,625 ; IF2021 5,141; MNiSW points 70, Q2

A23. Dorota Chelminiak, **Marta Ziegler-Borowska,** Halina Kaczmarek*. Synthesis of magnetite nanoparticles coated with poly (acrylic acid) by photopolymerization. *Mat. Lett.* , **2016**, *164*, 464-467; doi: /10.1016/j.matlet.2015.11.023
IF2015 2,572 ; IF2021 3,574; MNiSW points 70, Q2

A24. Joanna Skopinska-Wisniewska*, Joanna Kuderko, Anna Bajek, Małgorzata Maj, Alina Sinkowska, **Marta Ziegler-Borowska**. Collagen/elastin hydrogels cross-linked by squaric acid, . *Mat. Sci. Eng.*: *C*, **2016**, *60*, 100-108; doi: 10.1016/j.msec.2015.11.015
IF$_{2016}$ 4,164 ; IF$_{2021}$ 8,457; MNiSW points 140, Q1

A25. Tomasz Siódmiak, Debby Mangelings, Yvan Vander Heyden, **Marta Ziegler-Borowska**, Michał Piotr Marszałł*. High enantioselective novozyme 435-catalyzed esterification of (R, S)-flurbiprofen monitored with a chiral stationary phase. *Appl. Biochem. Biotechnol.*, **2015**, *175*, 2769-2785; doi: 10.1007/s12010-014-1455-4
IF$_{2015}$ 1.606 ; IF$_{2021}$ 3.094; MNiSW points 70, Q3

A26. Dorota Chelminiak, **Marta Ziegler-Borowska,** Halina Kaczmarek*. Polymer coated magnetite nanoparticles for biomedical applications. Part II. Fe_3O_4 nanoparticles coated by synthetic polymers. *Polymers*, **2015**, *60*, 87-94;
IF$_{2015}$ 0.718 ; IF$_{2021}$ 1.528; MNiSW points 70, Q4

A27. Dorota Chelminiak, **Marta Ziegler-Borowska,** Halina Kaczmarek*. Polymer coated magnetite nanoparticles for biomedical applications. Part I. Preparation of nanoparticles Fe_3O_4 coated by polysaccharides. *Polymers*, **2015**, *60*, 12-17;
IF$_{2015}$ 0.718 ; IF$_{2021}$ 1.528; MNiSW points 70, Q4

A28. Marta Ziegler-Borowska*, Marta Chylinska, Dariusz Kedziera, Anna Kaczmarek-Kedziera. Simple and efficient synthesis with theoretical calculations of novel N-halamine monomers. *Desig. Monom. Polym.* , **2014**,*17*, 528-534; doi: 10.1080/15685551.2013.867580
IF$_{2014}$ 2,780 ; IF$_{2021}$ 3,718; MNiSW points 40, Q2

A29. Marta Chylińska, **Marta Ziegler-Borowska,** Halina Kaczmarek*, Aleksandra Burkowska, Maciej Walczak, Przemysław Kosobucki. Synthesis and biocidal activity of novel N-halamine hydantoin-containing polystyrenes. *e-Polymers*, **2014**, *14*, 15-25; doi:10.1515/epoly-2013-0010
IF$_{2014}$ 0.569 ; IF$_{2021}$ 3.074; MNiSW points 40, Q2

A30. Tomasz Siódmiak, **Marta Ziegler-Borowska**, Michał Piotr Marszałł*, Lipase-immobilized magnetic chitosan nanoparticles for kinetic resolution of (R,S)-ibuprofen, J. *Mol. Cat. B: Enzymatic*, **2013**, *94*, 7-14; doi: 10.1016/j.molcatb.2013.04.008
IF$_{2013}$ 2.745 ; IF$_{2021}$ 2.269; MNiSW points 70, Q2

A31. Halina Kaczmarek*, Marta Chylińska, **Marta Ziegler-Borowska**. Thermal properties of novel polymers based on poly(hydantoin-methyl-p-styrene) and their

substrates. *J. Therm. Anal. Calorim*., **2012**, *110*, 1315-1326; doi: 10.1007/s10973-011-2076-6
IF$_{2012}$ 1,982 ; IF$_{2020}$ 4,626; MNiSW points 70, Q2

A32. Halina Kaczmarek*, **Marta Ziegler-Borowska,** Marta Chylińska, Jolanta Kowalonek, Magdalena Wolnicka. Effect of azobenzene derivatives on the photochemical stability of poly (methyl methacrylate) films. *Polym. Deg. Stab.,* **2012**, *97*, 1305-1313; doi: 10.1016/j.polymdegradstab.2012.05.021
IF$_{2012}$ 2,770 ; IF$_{2021}$ 5,204; MNiSW points 100, Q1

A33. Mariusz J Bosiak, Judyta A Jakubowska, Krzysztof B Aleksandrzak, Szymon Kamiński, Anna Kaczmarek-Kędziera, **Marta Ziegler-Borowska,** Dariusz Kędziera, Jörg Adams. Synthesis of a new class of highly fluorescent aryl-vinyl benzo [1, 2-b: 4, 5-b'] difuran derivatives. *Tetrahedron Lett*., **2012**, *53*, 3923-3926; doi: 10.1016/j.tetlet.2012.05.087
IF$_{2012}$ 2,397 ; IF$_{2021}$ 2,032; MNiSW points 70, Q2

A34. Marta Ziegler-Borowska, Marzena Ucherek, Jolanta Kutkowska, Liliana Mazur, Bożena Modzelewska-Banachiewicz, Dariusz Kędziera, Anna Kaczmarek-Kędziera*, Reaction of N3-phenylbenzamidrazone with cis-1, 2-cyclohexanedicarboxylic anhydride. *Tetrahedron Lett*., **2010**, *51*, 2951-2955; doi: 10.1016/j.tetlet.2010.03.116
IF$_{2010}$ 2.618 ; IF$_{2021}$ 2.032; MNiSW points 70, Q2

B-list journals:

A35. Radosław Szczepański, Laura Gadomska, Marek Michalak, Paweł Bakun, Kacper Pawlak, Tomasz Gośliński*, **Marta Ziegler-Borowska**, Beata Czarczyńska-Goślińska, Chitosan-derivatives in combinations with selected porphyrinoids as novel hybrid materials for medicine and pharmacy, *Progress on Chemistry and Application of Chitin and its Derivatives*, **2020**, *25*, 63-78.
MNiSW credits 70

7.3 Further research perspectives

Further scientific plans arise directly from my interests and are related to the fact that since 2019 the Medicinal Chemistry Team is part of the Toruń Centre of Excellence 'Towards Personalised Medicine'. The experience I have gained in both the synthesis and characterisation of new polymeric materials, nanotechnology and broadly defined medical and pharmaceutical chemistry and pharmaceutical chemistry allows the start of new projects related to selective drug delivery,

particularly from the anticancer drug group, and to the synthesis of materials based on natural polymers capable of binding specific proteins such as glycoproteins. Work related to the synthesis of the above-mentioned materials has already begun as part of preliminary studies for grant applications in preparation.

The aim of future projects is to be able to obtain nanomaterials based on biopolymers capable of penetrating biological membranes and carrying active substances for clinical use in anticancer therapy. This is a continuation and development of the subject matter already hinted at in publication **H9**. I assume that the new systems will achieve selectivity towards healthy cells through a combination of magnetic, and photochemical properties and response to changes in ambient pH. The nanostructures obtained in this project will be based on human and animal proteins, as well as polysaccharides. The addition of magnetite should ensure, on the one hand, the selective penetration of the nanoparticles into cancer cells, due to their high demand for iron compounds, and, on the other hand, will allow the material to be guided directly to the tumour-affected tissue by an external magnetic field. At the same time, taking advantage of changes in the metabolism of tumour cells resulting in a decrease in pH in relation to healthy tissue, it will be possible to selectively release the cytostatic by hydrolysis of the bond linking the drug to the carrier. The research will be carried out in collaboration with the teams that make up BRAIN, Dr. Emilia Piosik from the Poznań University of Technology, Prof. Tomasz Gośliński from the Faculty of Pharmacy at the Poznań University of Medical Sciences, as well as Dr. Tania Limongi (Department of Applied Science and Technology, Turin University of Technology) and Prof. Petr Zimcik (Department of Pharmaceutical Chemistry and Drug Analysis, Faculty of Pharmacy in Hradec Kralove).

Another line of research that has also already been initiated is the synthesis of new polysaccharide composites with active substances of plant origin capable of forming hydro or oleogels as potential materials for the treatment of hard-to-heal wounds. This is an extension of the topics signalled in publications **A5** and **A3**. The materials obtained will have the ability to interact with proteins involved in the wound healing process (glycoprotein, von Willebrand factor, thrombin) and will contain added active substances of natural origin to accelerate the healing process, inhibit chronic inflammation and prevent infection. In addition, an innovative 3D biological model approach will be used in the biological testing of the materials. The work will be carried out in collaboration with FF Med Sp. z o.o.

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