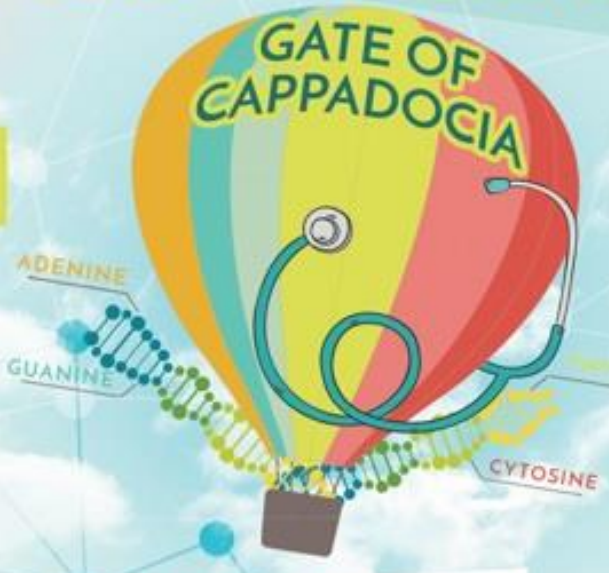
INTERNATIONAL CONGRESS ON

BIOLOGICAL AND MEDICAL SCIENCES

NİĞDE/TURKEY/2018



POSTER AWARDS

ORAL PRESENTATION AWARDS

ABSTRACT DEADLINE

31.07.2018

TREND TOPICS OF THE CONGRESS

Aging
Anatomy
Biochemistry
Biophysics
Cancer Biology
Histology
Microbiology
Molecular Biology
Pharmacology
Physiology
Reproductive Biology
Traditional and complementary medicine

31 OCTOBER-3 NOVEMBER 2018

ŞEHİT ÖMER HALİSDEMİR CONGRESS CENTER

Mail: ibamsc2018@gmail.com

Web: www.ohu.edu.tr/icbms2018

Social Media: /ibamsc2018

International Congress on Biological and Medical Sciences 2018

Life Science and Medicine

31 October-03 November 2018

NİGDE ÖMER HALİSDEMİR UNIVERSITY

TURKEY

PROCEEDING BOOK

The responsibility of the full papers contained in this book belongs to their authors

International Congress on Biological and Medical Sciences 2018
31 October-03 November 2018, Nigde / TURKEY
www.ohu.edu.tr/icbms2018

ORGANIZING COMMITTEE

HONORARY CHAIRMEN

Prof. Dr. Muhsin KAR (Rector of Niğde Ömer Halisdemir University)

CHAIRMAN OF CONGRESS

Dr. Zeliha SELAMOGLU

CONGRESS SECRETARIAT

Dr. Eylem TASKIN GUVEN

ORGANIZING COMMITTEE MEMBERS

Dr. Uner KAYABAS

Dr. Adnan UNALAN

Dr. Celal GUVEN

Dr. Fatih Mehmet GUR

Dr. Arife Zuhal DEGIRMENCIOGLU

Dr. Betül OZALTUN

Dr. Mehmet Erman ERDEMLI

Dr. Mustafa DOGAN

SCIENTIFIC COMMITTEE MEMBERS

Dr. Abdullah ARPACI	Mustafa Kemal University, Turkey
Dr. Abdurrahman AKTUMSEK	Selçuk University, Turkey
Dr. Ahmet AKSOY	Gazi University, Turkey
Dr. Akifumi KISHI	University of Tokyo, Japan
Dr. Anna PEKSA	Wroclaw University, Poland
Dr. Antonio SUREDA GOMILA	University of the Balearic Islands, Spain
Dr. Ardalan PASDARAN	Shiraz University, Iran
Dr. Atanas G. ATANASOV	University of Vienna, Austria
Dr. Aydın GIRGIN	Fırat University, Turkey
Dr. Aysun BAY KARABULUT	Yıldırım Beyazıt University, Turkey
Dr. Azhar RASUL	Government College University, Pakistan
Dr. Belgin BUYUKAKILLI	Mersin University, Turkey
Dr. Belgin SUSLEYICI	Marmara University, Turkey
Dr. Belma TURAN	Ankara University, Turkey
Dr. Can DEMIREL	Gaziantep University, Turkey
Dr. Cem EKMEKCIOGLU	Medical University, Austria
Dr. Cemil SERT	Harran University, Turkey
Dr. Deniz ERBAS	Gazi University, Turkey
Dr. Engin ULUKAYA	İstinye University, Turkey
Dr. Eva URGEOVA	University of SS Cyril and Methodius, Slovakia
Dr. Farhat JABEEN	Government College University, Pakistan
Dr. Francesca CIGNARELLA	Washington University, USA
Dr. Gabriel PLAVAN	University of Iasi, Romania
Dr. Gamal BADR	Assiut University, Egypt
Dr. Hande YAPISLAR	Acıbadem University, Turkey
Dr. Handan AKCAKAYA	Istanbul University, Turkey
Dr. Harika GOZUKARA BAG	İnönü University, Turkey
Dr. Hasan AKGUL	Akdeniz University, Turkey
Dr. Hikmet GECKIL	İnönü University, Turkey
Dr. Ilkay ERDOGAN ORHAN	Gazi University, Turkey
Dr. Ilhami BERBER	Erciyes University, Turkey
Dr. Ismail GUNAY	Çukurova University, Turkey
Dr. Ismet YILMAZ	İnönü University, Turkey
Dr. Kazim SAHIN	Fırat University, Turkey
Dr. Lejla RIDANOVIC	Dzemal Bijedic University of Mostar, Bosnia and Herzegovina
Dr. Leyla SAHIN	Mersin University, Turkey
Dr. Maria DAGLIA	The University of Pavia, Italy

SCIENTIFIC COMMITTEE MEMBERS

Dr. Mehmet Can AKYOLCU	İstanbul University, Turkey
Dr. Mehmet GUL	İnönü University, Turkey
Dr. Mehmet Rustu KARAMAN	Yüksek İhtisas University, Turkey
Dr. Mehmet TUZCU	Fırat University, Turkey
Dr. Mehmet VAROL	Muğla Sıtkı Koçman University, Turkey
Dr. Murat TELLI	Bolu Abant İzzet Baysal University, Turkey
Dr. Mustafa SEVINDIK	Akdeniz University, Turkey
Dr. Muhsin KONUK	Üsküdar University, Turkey
Dr. Mustafa DJAMGOZ	Imperial College London, England
Dr. Nady BRAIDY	University of New South Wales, Australia
Dr. Necati TMURKAAN	Fırat University, Turkey
Dr. Neslihan ABACI	İstanbul University, Turkey
Dr. Nurcan DURSUN	Erciyes University, Turkey
Dr. Pelin YAZGAN	Okan University, Turkey
Dr. Ramin Ekhteiari SALMAS	İstanbul Teknik University, Turkey
Dr. Ravichandran RAMASAMY	New York University, USA
Dr. Sachiyo ABURATANI	National Institute of Advanced Industrial Science and Technology, Japan
Dr. Salih Tunc KAYA	Düzce University, Turkey
Dr. Sami SIMSEK	Fırat University, Turkey
Dr. Samra MEDEDOVIC	Dzemal Bijedic University of Mostar, Bosnia and Herzegovina
Dr. Sanel RIDANOVIC	Dzemal Bijedic University of Mostar, Bosnia and Herzegovina
Dr. Sayad KOCAHAN	Bakû State University, Azerbaijan
Dr. Seyed Mohammad NABAVI	Iran University of Medical Sciences, Tehran, Iran
Dr. Sema TIMURKAAN	Fırat University, Turkey
Dr. S.D. SARASWATHY	Bharathidasan University, India
Dr. Serdar SONMEZ	Adıyaman University, Turkey
Dr. Sergey SHITYAKOV	University Hospital Würzburg, Germany
Dr. Seyhun SOLAKOGLU	İstanbul University, Turkey
Dr. Solomon HABTEMARIAM	University of Greenwich, England
Dr. Sudin BHATTACHARYA	Chittaranjan National Cancer Institute West Bengal, India
Dr. Thelma Veronica POGGIO	Hospital de Niños Ricardo Gutierrez, Argentina
Dr. Tibor MALIAR	University of SS Cyril and Methodius, Slovakia
Dr. Utku AVCI	Recep Tayyip Erdoğan University, Turkey
Dr. Viera HORVATHOVA	University of SS Cyril and Methodius, Slovakia
Dr. William A. COETZEE	New York University, USA
Dr. Yusuf SEVGILER	Adıyaman University, Turkey

ORAL PRESENTATION

Development of Molecular Imprinting Technology and The Effective Use of Molecular Imprinted Polymers

Suleyman Serdar Alkanli[1]*, Fulya Dal Yontem[2], Merve Yasar[3], Celal Guven[4], Nilhan Kayaman Apohan[3], Zerrin Aktas[5], Memet Vezir Kahraman[3], Mustafa Oral Oncul[6], Handan Akcakaya[1]

[*1]Istanbul University, Istanbul Faculty of Medicine, Department of Biophysics, Istanbul, Turkey
[2]Halic University, Faculty of Medicine, Department of Biophysics, Istanbul, Turkey
[3]Marmara University, Faculty of Arts and Sciences, Department of Chemistry, Istanbul, Turkey
[4]Nigde Omer Halisdemir University, Faculty of Medicine, Department of Biophysics, Nigde, Turkey
[5]Istanbul University, Istanbul Faculty of Medicine, Department of Medical Microbiology, Istanbul, Turkey
[6]Istanbul University, Istanbul Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey

*Corresponding author e-mail: alkanliserdar@gmail.com

Abstract

Highly selective molecules used for antibodies or enzymes have great importance in chemistry, diagnosis and biology. However, the production of these natural receptors is difficult and expensive. Their longevity and applicability are also limited. Molecular imprinting technique (MIT) has been developed to overcome these limitations. The functional groups of the polymerizable monomers are combined with the template molecule to enable the desired selectivity. After polymerization in the presence of cross-linkers, template molecules in the polymer are removed to obtain molecularly imprinted polymers (MIPs) recognizing the size, shape and surface chemistry of the template molecule. Polymers that are selective to template molecule are cheaper, simpler and more durable than their counterparts. Polymers with different properties can be produced using a wide variety of monomers. MIT development has been ongoing for over 30 years and it's an effective method for preparing synthetic molecular recognition systems with similar binding properties like natural antibodies. MIPs used as initial separation methods are polymers, synthetic enzymes, biological receptors and biosensors with catalytic activity under the influence of progressive studies and technological developments. MIT can be adapted to the Enzyme Linked Immunosorbent Assay (ELISA), an immunological assay based on antibody-antigen interaction. MIPs are used in drug development studies, drug delivery and medicine as biomimetic antibodies. In our study, we showed that MIP imprinted against template molecule, can bind its target molecule in *in vitro* cell culture assays and can also be used in an ELISA.

Keywords: Molecular Imprinted Polymer, Biomimetic Antibody.

1. Introduction

MIPs have gained importance due to their wide applications in chemical sensing, separation, drug delivery, and extraction [1]. In the presence of template molecule, MIPs can be synthesized by co-polymerization of functional monomers and cross-linkers. The cross-linkers have function of stabilizing the binding sites after removal of the template molecule and forming recognition cavities for MIPs to detect similar molecules [2]. MIPs have important properties, such as specific recognition and high stability at high temperatures, compared to other analysis techniques [3]. In antibody-antigen interactions, , the antibody recognizes an epitope of the antigen [4–6]. The use of commercially available antibodies for isolation and purification is quite expensive and difficult to store for long periods [7]. MIPs obtained by the polymerization process around the surface of template molecule with the cross-linker can perform an antibody-like function after template molecule has been removed and recognize the same molecule using specific binding sites [8]. MIPs can now be used in a wide range of applications, such as separation (e.g., chromatography, capillary electrophoresis, solid-phase extraction, and membrane separation, etc.), immunoassays, antibody mimics, artificial enzymes, (bio)sensors, catalysis, organic synthesis, drug delivery and drug development [1].

2. Materials and Methods

Materials

Template Molecules

The purpose of molecular imprinting is to produce MIPs with affinity and specificity that are comparable to those of biological receptors, and ultimately alter these biological entities in real applications. An ideal template molecule should contain functional groups that do not inhibit polymerization, exhibit excellent chemical stability during the polymerization reaction and contain functional groups capable of complexing with functional monomers [2]. MIPs have recently been successfully applied for the identification and detection of various small organic molecules. In addition, large structured species such as viruses and cells have also been reported for MIPs [9–12]. However, great challenges remain for imprinting of proteins and other bio-macromolecules [13, 14].

Functional Monomers

Functional monomers providing functional groups have a role in forming a pre-polymerization complex with the template molecule. Therefore, it is important to select suitable functional monomers which can interact strongly with template molecule and may form specific donor-receptor or antibody-antigen complexes prior to polymerization [1]. Among the functional monomers, methacrylic acid (MAA) has been used as a functional monomer because of its hydrogen bonding, receptor properties and its dimerization modestly increases its imprinting effect [15]. It was also shown that high molar fractions of MAA will result in large pore size of the polymeric materials and further enhance the binding capacity of the polymers [16].

Cross-linkers

In polymerization process, cross-linkers are used to fix the functional monomers around template molecules, so that even after removal of template molecules, a highly crosslinked solid polymer is formed. The amount and type of cross-linker has a significant effect on selectivity and binding capacity of MIPs [17].

Solvents

The fluorogenic solvents generally act as dispersing media and pore forming agents in the polymerization process therefore play an important role in polymerization. Generally, the solvents used for the MIP synthesis are 2-methoxyethanol, methanol, tetrahydrofuran (THF), acetonitrile, dichloroethane, chloroform, N, N-dimethylformamide (DMF) and toluene [18].

Initiators

Most MIPs are widely prepared by free radical polymerization (FRP), photo-polymerization and electro-polymerization. FRP can be thermally or photo-chemically initiated for various functional groups and templates. As well as peroxy compounds, azo compounds are also widely used as initiators. One of is the azo compound is azobisisobutyronitrile (AIBN), which is optimally used at decomposition temperatures around 50-70 °C. In order to achieve the polymerization reaction, it is very important to remove dissolved oxygen from polymerization solutions prior to proliferation. Cleaning the oxygen can be achieved by bubbling an inert gas such as nitrogen or argon [1].

Preparation of MIPs

Molecular imprinting is carried out by polymerization of functional monomer around the template molecule in the presence of cross-linker [17]. First, template molecule-monomer complex is obtained by using different molecular imprinting technologies between selected molecule and complementary functional monomers [19]. After the polymerization reaction around the complex, template molecule is extracted and as a result, the three-dimensional polymer with complementary binding sites is obtained with the geometry and position of template molecule functional groups. In the production of MIPs, two main methods are usually used based on covalent and non-covalent interactions between template molecule and functional monomers. Covalent imprinting provides the formation of functional monomer residues in the imprinted cavities. However, covalent imprinting is considered to be a less flexible method because of its limited reversible reactions. In addition, the strong covalent interactions result in slow binding and dissociation, making it difficult to reach the thermodynamic equilibrium [20]. Non-covalent imprinting may occur by ionic interactions, hydrogen bonding, van der Waals forces and π-π interactions. The most common non-covalent interaction is the hydrogen bonding between MAA groups and primary amines in non-polar solvents [21]. Recently, non-covalent imprinting has become the most popular synthesis strategy due to its ease and quickness of binding and extraction.

Characterization Methods

Morphologic properties of MIPs are widely studied by scanning electron microscopy (SEM) and transmission electron microscopy (TEM). In addition, atomic force microscopy (AFM) and various fluorescence techniques are also used for the characterization of thin film MIPs. However, there has been a recent trend in spectroscopic studies of ligand-MIP interactions [1].

3. Results and Discussion

In this study, fundamentals of MIPs are summarized briefly and production processes are emphasized. Solid phase extraction (SPE) is widely used for MIPs called molecular printed SPEs. Molecularly imprinted SPE absorbers are available in a variety of forms such as cartridges, discs, SPE pipette tip, 96-well SPE microtiter plates [22]. Solid phase micro extraction (SPME) is widely used for sample preparation in analytical laboratories due to its simple, solvent-free and short-term results. Stir bar sorption extraction (SBSE) derived from SPME has a similar extraction mechanism

like SPME. SBSE has some advantages as high enrichment factor, reproducibility, high adsorption capacity and solvent-free and has been applied in environment, food and biological samples [23, 24]. In addition to their wide application areas in pre-treatment techniques, MIPs are also used as stationary phases in chromatography techniques such as HPLC [25], capillary electrochromatography (CEC) [26] and capillary LC (CLC) [27]. On the other hand, similar tests have been developed with enzyme-linked immunosorbent assay (ELISA) by coating microplate wells with MIPs [28]. MIP-based sensors are first proposed by Mosbach for specific binding of vitamin K_1 to the silicon surface by surface-imprinting method and using an optical surface ellipsometry [29]. In addition, MIP-based sensors can be developed by designing and preparing MIP particles or films. MIPs are widely applicable but their high volume production and large-scale applications are rarely reported. For these reasons, computational and combinatorial tools are required for synthetic MIPs.

5. Conclusion

This study shows that molecularly imprinted polymers can be used in chemical detection, separation, drug delivery and extraction applications. In addition, MIPs can be used in pseudo ELISA assays however further investigation is needed to produce high volume and large scale of MIPs.

Acknowledgements

This work was supported by the Scientific and Technological Research Council of Turkey (TUBITAK) (project no: 115S224)

Conflicts of Interest

There is no conflict of interest

References

[1] Chen, L., Xiaoyan, W., Wenhui, L., Xiaqing, W., & Jinhua L. (2016). Molecular imprinting: Perspectives and applications. Chemical Society Reviews.

[2] Chen, L., Shoufang, X., & Jinhua, L. (2011). Recent advances in molecular imprinting technology: Current status, challenges and highlighted applications. Chemical Society Reviews.

[3] Li, X., Baoliang, Z., Wie, L., Xingfeng, L., Xinlong, F., Lei, T., Hepeng, Z., & Qiuyu, Z. (2014). Preparation and characterization of bovine serum albumin surface-imprinted thermosensitive magnetic polymer microsphere and its application for protein recognition. Biosensors and Bioelectronics, 51, 261–267.

[4] Mariuzza, R A, Phillips, S.E. & Poljak, R. J. (1987). The structural basis of antigen-antibody recognition. Annu Rev Biophys Biophys Chem, 16, 139–159.

[5] Rini, J. M., Schulze-Gahmen, U., & Wilson, I. A. (1992). Structural evidence for induced fit as a mechanism for antibody-antigen recognition. Science, 255(5047), 959-965.

[6] Van Regenmortel, M. H. (2014). Specificity, polyspecificity, and heterospecificity of antibody-antigen recognition. Journal of Molecular Recognition, 27(11), 627-639.

[7] Zhang, Z., Guan, Y., Li, M., Zhao, A., Ren, J., & Qu, X. (2015). Highly stable and reusable imprinted artificial antibody used for in situ detection and disinfection of pathogens. Chemical science, 6(5), 2822-2826.

[8] Vasapollo, G., Sole, R. D., Mergola, L., Lazzoi, M. R., Scardino, A., Scorrano, S., & Mele, G. (2011). Molecularly imprinted polymers: present and future prospective. International journal of molecular sciences, 12(9), 5908-5945.

[9] Hayden, O., & Dickert, F. L. (2001). Selective microorganism detection with cell surface imprinted polymers. Advanced Materials, 13(19), 1480-1483.

[10] Takátsy, A., Kilár, A., Kilár, F., & Hjertén, S. (2006). Universal method for synthesis of artificial gel antibodies by the imprinting approach combined with a unique electrophoresis technique for detection of minute structural differences of proteins, viruses, and cells (bacteria): Ia. Gel antibodies against proteins (transferrins). Journal of separation science, 29(18), 2802-2809.

[11] Cai, D., Ren, L., Zhao, H., Xu, C., Zhang, L., Yu, Y., ... & Naughton, M. J. (2010). A molecular-imprint nanosensor for ultrasensitive detection of proteins. Nature nanotechnology, 5(8), 597.

[12] Zhang, Z., Li, M., Ren, J., & Qu, X. (2015). Cell-Imprinted Antimicrobial Bionanomaterials with Tolerable Toxic Side Effects. Small, 11(11), 1258-1264.

[13] Li, S., Cao, S., Whitcombe, M. J., & Piletsky, S. A. (2014). Size matters: Challenges in imprinting macromolecules. Progress in Polymer Science, 39(1), 145-163.

[14] Zhang, W., He, X. W., Chen, Y., Li, W. Y., & Zhang, Y. K. (2011). Composite of CdTe quantum dots and molecularly imprinted polymer as a sensing material for cytochrome c. Biosensors and Bioelectronics, 26(5), 2553-2558.

[15] Zhang, Y., Song, D., Lanni, L. M., & Shimizu, K. D. (2010). Importance of functional monomer dimerization in the molecular imprinting process. Macromolecules, 43(15), 6284-6294.

[16] Golker Golker, K., Karlsson, B. C., Olsson, G. D., Rosengren, A. M., & Nicholls, I. A. (2013). Influence of composition and morphology on template recognition in molecularly imprinted polymers. Macromolecules, 46(4), 1408-1414.

[17] Yan, H., & Row, K. H. (2006). Characteristic and synthetic approach of molecularly imprinted polymer. International journal of molecular Sciences, 7(5), 155-178.

[18] Gladis, Joseph M., and Talasila P. Rao. (2004). Effect of porogen type on the synthesis of uranium ion imprinted polymer materials for the preconcentration/separation of traces of uranium. Microchimica Acta 146: 251–258.

[19] Gladis, J. M., & Rao, T. P. (2004). Effect of porogen type on the synthesis of uranium ion imprinted polymer materials for the preconcentration/separation of traces of uranium. Microchimica Acta, 146(3-4), 251-258.

[20] Alexander, C., Andersson, H. S., Andersson, L. I., Ansell, R. J., Kirsch, N., Nicholls, I. A., & Whitcombe, M. J. (2006). Molecular imprinting science and technology: a survey of the literature for the years up to and including 2003. Journal of Molecular Recognition: An Interdisciplinary Journal, 19(2), 106-180.

[21] Schirhagl, R. (2013). Bioapplications for molecularly imprinted polymers. Analytical chemistry, 86(1), 250-261.

[22] Tóth, B., & Horvai, G. (2010). Chromatography, solid-phase extraction, and capillary electrochromatography with MIPs. In Molecular Imprinting (pp. 267-306). Springer, Berlin, Heidelberg.

[23] Gilart, N., Marcé, R. M., Borrull, F., & Fontanals, N. (2014). New coatings for stir-bar sorptive extraction of polar emerging organic contaminants. TrAC Trends in Analytical Chemistry, 54, 11-23.

[24] Baltussen, E., Sandra, P., David, F., & Cramers, C. (1999). Stir bar sorptive extraction (SBSE), a novel extraction technique for aqueous samples: theory and principles. Journal of

Microcolumn Separations, 11(10), 737-747.

[25] Jia, M., Qin, L., He, X. W., & Li, W. Y. (2012). Preparation and application of lysozyme imprinted monolithic column with dopamine as the functional monomer. Journal of Materials Chemistry, 22(2), 707-713.

[26] Zaidi, S. A. (2013). Dual-templates molecularly imprinted monolithic columns for the evaluation of serotonin and histamine in CEC. Electrophoresis, 34(9-10), 1375-1382.

[27] Zhang, Z., Wu, R. A., Wu, M., & Zou, H. (2010). Recent progress of chiral monolithic stationary phases in CEC and capillary LC. Electrophoresis, 31(9), 1457-1466.

[28] Chianella, I., Guerreiro, A., Moczko, E., Caygill, J. S., Piletska, E. V., De Vargas Sansalvador, I. M. P., ... & Piletsky, S. A. (2013). Direct Replacement of Antibodies with Molecularly Imprinted Polymer Nanoparticles in ELISA Development of a Novel Assay for Vancomycin. Analytical chemistry, 85(17), 8462-8468.

[29] Andersson, L. I., Mandenius, C. F., & Mosbach, K. (1988). Studies on guest selective molecular recognition on an octadecyl silylated silicon surface using ellipsometry. Tetrahedron letters, 29(42), 5437-5440.