ANEXA 3b

UNIVERSITATEA POLITEHNICA DIN BUCURESTI

FIŞA DE VERIFICARE A ÎNDEPLINIRII STANDARDELOR DE SUSŢINEREA TEZEI DE ABILITARE

CANDIDAT STANCU IZABELA-CRISTINA
Depart. de Bioresurse şi Ştiinta Polimerilor Fac. de Chimie Aplicată şi Ştiinţa Materialelor

<table>
<tr><th>Condiţii</th><th colspan="2">Îndeplinire condiţii</th></tr>
<tr><td>A. Doctor</td><td colspan="2">Diploma de Doctor în domeniul Chimie, nr 407 din 01.06.2004, seria C/Nr 0009282, emisă de Universitatea Politehnica din Bucureşti în baza OMEC nr. 3876 din 19.05.2004</td></tr>
<tr><td>B. Îndeplinirea standardelor minime naţionale conform OMECTS nr. 6129/20.12.2016;
Profesor universitar, Comisia CNATDCU nr. 8</td><td colspan="2">Standarde indeplinite, conform Comisiei CNATDCU Anexa nr. 8 - Inginerie Chimică, Inginerie Medicală, Ştiinţa Materialelor si Nanomateriale
Anexată: Fişa de calcul si de sustinere a indeplinirii standardelor minimale specifice domeniului, in acord cu realizarile mentionate:</td></tr>
<tr><td>Condiţii minimale profesor [Punctaj]</td><td>Minim prevăzut</td><td>Realizat la data depunerii dosarului 10.06.2020</td></tr>
<tr><td>a) NTOP ≥ 4 ; NTOP = număr total de articole în reviste ISI situate in top 25% (zona roșie) în calitate de autor principal. Situația revistelor în top 25% se judecă în cazul cel mai convenabil pentru candidat, fie la momentul publicării fie la data înscrierii la concurs</td><td>4</td><td>7
(Tabel 3b.1)</td></tr>
<tr><td>b) NP ≥ 20 ; NP = număr articole în reviste ISI la care candidatul este autor principal (prim autor sau autor de corespondenţă)</td><td>20</td><td>25
(Tabel 3b.1)</td></tr>
<tr><td>c) FIC≥ 30 ; FIC = factor de impact cumulat (suma factorilor de impact ai revistelor)</td><td>30</td><td>65.597
(Tabel 3b.1)</td></tr>
<tr><td>d) NC ≥ 120
NC = număr total de citări (din baza SCOPUS)</td><td>120</td><td>459
(Tabel 3b.3)</td></tr>
<tr><td>e) NCO > = 1 (în calitate de Director proiect)</td><td>1</td><td>5
(Tabel 3b.2)</td></tr>
<tr><td rowspan="2">C. Atestarea studiilor (diploma + Foi Matricole) şi a altor realizari profesionale</td><td colspan="2">Diplomă de Licenţă, în domeniul Inginerie Chimică Nr.1889 din 22.I.2001 emisă de Universitatea Politehnica din Bucureşti</td></tr>
<tr><td colspan="2">Diplomă de studii post-doctorale în domeniul Ştiinţe Exacte-Chimie, emisă de Universitatea POLITEHNICA din Bucureşti
____
Alte Certificate
Certificat de Absolvire pentru Nivelul I seria C, Nr. 0045266/11.02.2012 emis de Departamentul pentru pregatirea personalului didactic, Universitatea Politehnica din Bucuresti
Certificat de Absolvire pentru Nivelul II seria C, Nr. 0045319/11.02.2012 emis de Departamentul pentru pregatirea personalului didactic, Universitatea Politehnica din Bucuresti</td></tr>
</table>

Subsemnata STANCU IZABELA-CRISTINA, Departam. de Bioresurse si Stiinta Polimerilor, Facultatea de Chimie Aplicată şi Ştiinţa Materialelor, din Domeniul de Studii Univ. Inginerie Chimică, arondat Comisiei de Specialitate CNATDCU [OMECTS 6573/2012] Nr.8, COMISIA INGINERIE CHIMICĂ, INGINERIE MEDICALĂ, ŞTIINŢA MATERIALELOR ŞI NANOMATERIALE**, declar pe propria răspundere, cunoscând prevederile art. 292 privind falsul în declaraţii, din Legea 286/2009 - Codul Penal, că sunt indeplinite toate Standardele minimale prevăzute de Metodologia UPB 2013 actualizată în conformitate cu schimbarile de legislatie in domeniu in 2017 si 2018 pentru inscrierea la concurs si sustin veridicitatea informatiilor prezentate in dosar si in materialul de mai sus. Lucrarile considerate a fi incluse in Baza ISI Thomson Reuters sau in alte Baze de Date Internationale [BDI] sunt vizibile in aceste baze, in dreptul numelui candidatului, la aceasta data.**

Candidat, **Data**

………………………………………… 10.06.2020

IN CONTINUARE: Fişa de calcul si de susţinere a îndeplinirii standardelor minimale specifice domeniului, în acord cu realizările menţionate

CANDIDAT STANCU IZABELA-CRISTINA
Depart. de Bioresurse şi Ştiinta Polimerilor Fac. de Chimie Aplicată şi Ştiinţa Materialelor

Fişa de calcul si de susţinere a îndeplinirii standardelor minimale specifice domeniului, în acord cu realizările menţionate

ResearcherID: D-3788-2014 http://www.researcherid.com/rid/D-3788-2014
ORCID: http://orcid.org/0000-0003-0685-3947

Tabel 3b.1. Verificare criterii NP, FIC si NTOP

Nr.	**Lucrari**	**FI** La data depunere dosar, 10.06.20	**Nr. Autori**	**FIC**	**NP**	**NC**	**NTOP**
Articole ISI - autor principal							
1	*JCR IF 1 of 32 – Q1, MATERIALS SCIENCE, BIOMATERIALS; 3 of 80 – Q1, ENGINEERING, BIOMEDICAL la data depunere dosar (10.06.2020)* **Izabela-Cristina Stancu**, Robert Filmon, Corneliu Cincu, Bogdan Marculescu, Catalin Zaharia, Yves Tourmen, Michel Felix Basle, Daniel Chappard - Synthesis of methacryloyloxyethyl phosphate copolymers and in vitro calcification capacity, **BIOMATERIALS**, ISSN: 0142-9612, 25 (2), 205-213, WOS:000253619900005, DOI: 10.1016/S0142¬9612(03)00485¬X, Article	10,273	8	10,273	1	46	1
2	*JCR ESI Total citations – 52/369-Q1, MATERIALS SCIENCE, zona roșie la data depunere dosar (10.06.2020)* **Izabela-Cristina Stancu**, Robert Filmon, Florence Grizon, Catalin Zaharia, Corneliu Cincu, Michel Felix Basle, Daniel Chappard - The in vivo calcification capacity of a copolymer, based on methacryloyloxyethyl phosphate, does not favor osteoconduction, **JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A**, ISSN: 0021-9304, 69A (3), 584-589, 2004, WOS:000221418400024, EID 2-s2.0-2442650303, Article	3,221	7	3,221	1	16	1
3	Adriana Lungu, **Izabela-Cristina Stancu**, Edina Rusen, Bogdan Marculescu, Horia Iovu - Studies concerning the chemical immobilization of dendrimers on macroporous polymer matrix, **JOURNAL OF OPTOELECTRONICS AND ADVANCED MATERIALS**, ISSN: 1454-4164, 9 (11), 3454-3458, 2007, WOS:000251435200035	0,588	5	0,588	1	0	0

4	Noise reduction in surface plasmon resonance images, Fernandez-Gonzalez, A ; **Stancu, IC**; Butac, LM ; Salzer, R, **OPTOELECTRONICS AND ADVANCED MATERIALS-RAPID COMMUNICATIONS** 1(9) 452-456 2007, WOS:000253725200007	0,452	4	0,452	1	0	0
5	**Izabela-Cristina Stancu**, Alfonso Fernández-González, Livia Maria Butac, Reiner Salzer - Surface plasmon resonance imaging sensors based on mucin - antimucin interaction, **JOURNAL OF OPTOELECTRONICS AND ADVANCED MATERIALS**, ISSN: 1454-4164, 9 (9), 2696-2702, WOS:000249903600006	0,588	4	0,588	1	1	0
6	**Izabela-Cristina Stancu**, Alfonso Fernández-González, Reiner Salzer - SPR imaging antimucin-mucin bioaffinity based biosensor as label-free tool for early cancer diagnosis. Design and detection principle, **JOURNAL OF OPTOELECTRONICS AND ADVANCED MATERIALS**, ISSN: 1454-4164, 9 (6), 1883-1889, 2007, WOS:000247153900062	0,588	3	0,588	1	4	0
7	**Izabela-Cristina Stancu**, Pierre Layrolle, Helene Libouban, Robert Filmon, G Legeay, Corneliu Cincu, Michel Felix Basle, Daniel Chappard - Preparation of macroporous poly (2-hydroxyethyl) methacrylate with interconnected porosity, **JOURNAL OF OPTOELECTRONICS AND ADVANCED MATERIALS**, ISSN: 1454-4164, 9 (7), 2125-2129, 2007, WOS:000248583100034	0,588	8	0,588	1	4	0
8	Adriana Lungu, Edina Rusen, Livia Maria Butac, **Izabela-Cristina Stancu**, Epoxy-mediated immobilization of PAMAM dendrimers on methacrylic hydrogels, **DIGEST JOURNAL OF NANOMATERIALS AND BIOSTRUCTURES**, ISSN: 1842-3582, 4 (1), 97-107, 2009, WOS:000267327200013	0,638	4	0,638	1	11	0
9	**Izabela-Cristina Stancu**, Adriana Lungu, Edina Rusen, Alexandra Mocanu, Petrisor Zamora Iordache, Diana Maria Dragusin, Cosmin Cotrut, Eugeniu Vasile, Horia Iovu -Multifunctional Pamam-Surface Nanostructured Particles Organized in Multimeric Clusters. Potential Smart Delivery Vehicles of Bioactive Species Through a High Selective Amine-Thiol Bioconjugation Strategy, **DIGEST JOURNAL OF NANOMATERIALS AND BIOSTRUCTURES**, ISSN: 1842-3582,	0,638	9	0,638	1	0	0

	5 (4), 1077-1087, 2010, WOS:000286064000008						
10	*JCR IF 18 of 87- Q1, POLYMER SCIENCE la data depunere dosar (10.06.2020) si la data publicarii 16/79)* **Izabela-Cristina Stancu** - Gelatin hydrogels with PAMAM nanostructured surface and high density surface-localized amino groups, **REACTIVE AND FUNCTIONAL POLYMERS**, ISSN: 1381-5148, 70 (5), 314-324, 2010, WOS:000277557100008, DOI: 10.1016/j.reactfunctpolym.2010.02.005	3,074	1	3,074	1	18	1
11	Teodora Zecheru, Traian Rotariu, Edina Rusen, Bogdan Marculescu, Florin Miculescu, Laura Alexandrescu, Iulian Antoniac, **Izabela-Cristina Stancu -** Poly(2-hydroxyethyl methacrylate-co-dodecyl methacrylate-co-acrylic acid): Synthesis, physico-chemical characterisation and nafcillin carrier, **JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE**, ISSN: 0957-4530 21 (10), 2793-2804, 2010, WOS:000283371200009, DOI: 10.1007/s10856-010-4129-y	2,467	8	2,467	1	6	0
12	**Izabela-Cristina Stancu**, Diana Maria Dragusin, Eugeniu Vasile, Roxana Trusca, Iulian Antoniac, Dan Sorin Vasilescu- Porous calcium alginate-gelatin interpenetrated matrix and its biomineralization potential, **JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE**, ISSN: 0957-4530, 22 (3), 451-460, 2011, WOS:000289302600003, DOI: 10.1007/s10856-011-4233-7	2,467	6	2,467	1	25	0
13	Diana Maria Dragusin, Diana Elena Giol, Andrada Serafim, Eugeniu Vasile, Teodora Zecheru, **Izabela-Cristina Stancu-** Casein - PHEMA: In vitro formation of nanometric Ca-P Nuclei, **DIGEST JOURNAL OF NANOMATERIALS AND BIOSTRUCTURES**, ISSN: 1842-3582, 6 (4), 1909-1918, 2011, WOS:000300568100050	0,638	6	0,638	1	2	0
14	*JCR IF la data depunere dosar 10.06.20, 2 of 71 - Q1, CHEMISTRY, APPLIED, JCR IF 2018, 4 of 87 – Q1, POLYMER SCIENCE* Silvia Bubenikova, **Izabela-Cristina Stancu**, Lucia Kalinovska, Etienne Schacht, Evi Lippens, Heidi Declercq, Maria Cornelissen, Matteo Santin, Muriel Amblard, Jean Martinez, Chemoselective cross-linking of alginate with thiol-terminated peptides for tissue engineering applications, **CARBOHYDRATE POLYMERS**,	6,044	10	6,044	1	16	1

	ISSN: 0144-8617, 88 (4), 1239-1250, 2012, DOI: 10.1016/j.carbpol.2012.01.089, EID 2-s2.0-84859421108, WOS:000302979700017,						
15	*JCR IF 2012, 57/241 - Q1, MATERIALS SCIENCE, MULTIDISCIPLINARY – la data publicarii* Vasile Eugeniu, Serafim Andrada, Dragusin, Diana-Maria, Petrea Celina, Iovu Horia, **Stancu Izabela-Cristina** Apatite formation on active nanostructured coating based on functionalized gold nanoparticles, **JOURNAL OF NANOPARTICLES RESEARCH**, ISSN: 1388-0764, 14 (6), Article Number: 918, 14 pg, 2012, WOS:000305328900033	2,009	6	2,009	1	8	1
16	*JCR IF la data depunere dosar 10.06.2020, 15 of 87 – Q1, POLYMER SCIENCE* Diana-Maria Dragusin, Sandra Van Vlierberghe, Peter Dubruel, Manuel Dierick, Luc Van Hoorebeke, Heidi Declercq, Maria Cornelissen, **Izabela-Cristina Stancu**, Novel gelatin-PHEMA porous scaffolds for tissue engineering applications, **SOFT MATTER**, ISSN: 1744-683X, 8 (37), 9589-9602, 2012, WOS:000308095700013, DOI: 10.1039/c2sm25536g	3,399	8	3,399	1	41	1
17	**Izabela-Cristina Stancu**, Adriana Lungu, Diana-Maria Dragusin, Eugeniu Vasile, Celina Damian, Iovu Horia - Porous Gelatin-Alginate-Polyacrylamide Scaffolds with Interpenetrating Network Structure: Synthesis and Characterization, **SOFT MATERIALS**, ISSN: 1539-445X, 11(4), 384-393, 2013, DOI: 10.1080/1539445X.2011.642091, WOS:000326713300002	0,973	6	0,973	1	9	0
18	Andrada Serafim, Eugeniu Vasile, Horia Iovu, **Izabela-Cristina Stancu** - Self-assembled gold-dendrimer composite nanoparticles as surface nanostructuring features, **DIGEST JOURNAL OF NANOMATERIALS AND BIOSTRUCTURES**, ISSN: 1842-3582, 8 (2), 613-620, 2013, WOS:000322737500014	0,638	4	0,638	1	1	0
19	Andrada Serafim, Catalin Tucureanu, Daniela-Geta Petre, Diana-Maria Dragusin, Aurora Salageanu, Sandra Van Vlierberghe, Peter Dubruel, **Izabela-Cristina Stancu -** One-pot synthesis of superabsorbent hybrid hydrogels based on methacrylamide gelatin and polyacrylamide. Effortless control of hydrogel properties through composition design, **NEW JOURNAL OF CHEMISTRY**, ISSN: 1144-0546, 38 (7),	3,069	8	3,069	1	18	0

	3112-3126, 2014, DOI: 10.1039/c4nj00161c, WOS:000338117900053						
20	Andrada Serafim, Romain Mallet, Florence Pascaretti-Grizon, **Izabela-Cristina Stancu**, Daniel Chappard - Osteoblast-Like Cell Behavior on Porous Scaffolds Based on Poly(styrene) Fibers, **BIOMED RESEARCH INTERNATIONAL**, ISSN:2314-6133, Article Number: 609319, 6 pag, 2014, DOI: 10.1155/2014/609319, WOS:000338084700001	2,197	5	2,197	1	12	0
21	Eugeniu Vasile, Andrada Serafim, Daniela Petre, Diana Elena Giol, Peter Dubruel, Horia Iovu, **Izabela-Cristina Stancu** - Direct Synthesis and Morphological Characterization of Gold-Dendrimer Nanocomposites Prepared Using PAMAM Succinamic Acid Dendrimers: Preliminary Study of the Calcification Potential, **THE SCIENTIFIC WORLD JOURNAL**, ISSN: 1537-744X, Article Number: 103462, 15 pages, 2014, WOS:000330882600001	1,219	7	1,219	1	11	0
22	*JCR ESI Total citations – 2015, 24/520-Q1, CHEMISTRY – la data publicarii* Andrada Serafim, Sergiu Cecoltan, Adriana Lungu, Eugeniu Vasile, Horia Iovu, **Izabela-Cristina Stancu -** Electrospun fish gelatin fibrous scaffolds with improved bio-interactions due to carboxylated nanodiamond loading, **RSC ADVANCES**, ISSN: 2046-2069, 5 (116), 95467, 11 pages, 2015, DOI: 10.1039/c5ra14361f, WOS:000364907300009	3,049	6	3,049	1	5	1
23	Cecoltan, Sergiu; **Stancu, Izabela-Cristina**; Dragusin, Diana Maria; Serafim, Andrada; Lungu, Adriana; Tucureanu, Catalin; Caras, Iuliana; Tofan, Vlad Constantin; Salageanu, Aurora; Vasile, Eugeniu; Mallet, Romain; Chappard, Daniel; Coman, Cristin; Istodorescu, Mircea; Iovu, Horia, Nanocomposite particles with improved microstructure for 3D culture systems and bone regeneration, **JOURNAL OF MATERIALS SCIENCE-MATERIALS IN MEDICINE**, 28(10), Article Number: 153, 2017, 12 pages DOI: 10.1007/s10856-017-5966-8, WOS:000411111500009	2,467	15	2,467	1	2	0
24	Dragusin, Diana Maria; Curti, Filis; Cecoltan, Sergiu; Sarghiuta, Daniela; Butac, Livia Maria; Vasile, Eugeniu; Marinescu, Rodica; **Stancu, Izabela Cristina**, Biocomposites Based on Biogenous Mineral for Inducing Biomimetic Mineralization,	1,393	8	1,393	1	2	0

	MATERIALE PLASTICE, 54(2): 207-213, 2017, WOS:000408702100003						
25	Serafim, Andrada; Olaret, Elena; Cecoltan, Sergiu; Butac, Livia Maria; Balanuca, Brindusa; Vasile, Eugeniu; Ghica, Mihaela; **Stancu, Izabela Cristina**, Bicomponent Hydrogels Based on Methacryloyl Derivatives of Gelatin and Mucin with Potential Wound Dressing Applications, **MATERIALE PLASTICE**, 55(1): 68-74, 2018 WOS:000444129500015	1,393	8	1,393	1	3	0
	Articole ISI						
1	Guillaume Mabilleau, **Izabela-Cristina Stancu**, T Honore, G Legeay, Corneliu Cincu, Michel Felix Basle, Daniel Chappard- Effects of the length of crosslink chain on poly(2-hydroxyethyl methacrylate) (pHEMA) swelling and biomechanical properties, JOURNAL OF BIOMEDICAL MATERIALS RESEARCH - PART A, 77 (1), 35-42, 2006, WOS:000235945000005	3,221	7	0,460	0	44	0
2	Guillaume Mabilleau, Eric Aguado, **Izabela-Cristina Stancu**, Corneliu Cincu, Michel Felix Basle, Daniel Chappard- Effects of FGF-2 release from a hydrogel polymer on bone mass and microarchitecture, BIOMATERIALS, 29 (11), 1593-1600, WOS:000253619900005, EID 2-s2.0-38749123989,	10,273	6	1,712	0	39	0
3	Alexandra Mocanu, Bogdan Marculescu, Raluca Somoghi, Florin Miculescu, Cristian Boscornea, **Izabela-Cristina Stancu-** Fluorescence enhancement for the complex PAMAM-BSA in the presence of photonic crystal heterostructures, COLLOIDS AND SURFACES A-PHYSICOCHEMICAL AND ENGINEERING ASPECTS, 392 (1), 288-293, 2011, WOS:000298899300038	3,131	6	0,522	0	6	0
4	Adriana Lungu, Madalina G Albu, Nicoleta Florea, **Izabela-Cristina Stancu,** Eugeniu Vasile, Horia Iovu- The influence of glycosaminoglycan type on the collagen-glycosaminoglycan porous scaffolds, DIGEST JOURNAL OF NANOMATERIALS AND BIOSTRUCTURES, 6 (4), 1867-1875, 2011, WOS:000300568100046	0,638	6	0,106	0	11	0
5	Diana-Maria Dragusin, Andrada Serafim, Teodora Zecheru, **Izabela-Cristina Stancu**, Eugeniu Vasile, Ciupina- Casein - nanosized nucleator for in vitro mineralization, OPTOELECTRONICS AND ADVANCED MATERIALS-RAPID COMMUNICATIONS, ISSN: 2065-	0,452	6	0,075	0	0	0

	3824, 1842-6573, 5 (12), p:1320-1324, 2011, WOS:000298850400012						
6	Catalin Zaharia, Mihaela-Ramona Tudora, **Izabela-Cristina Stancu**, Bianca Galateanu, Adriana Lungu, Corneliu Cincu- Characterization and deposition behavior of silk hydrogels soaked in simulated body fluid, MATERIALS SCIENCE & ENGINEERING C-MATERIALS FOR BIOLOGICAL APPLICATIONS, 32 (4), 945-952, WOS:000303299300047	4,959	6	0,827	0	18	0
7	Andrada Serafim, Diana Maria Dragusin, Teodora Zecheru, Peter Dubruel, Daniela Petre, Lucian Toma Ciocan, Eugeniu Vasile, **Izabela-Cristina Stancu**- Gelatin hydrogels: Effect of ethylene oxide based synthetic crosslinking agents on the physico-chemical properties, DIGEST JOURNAL OF NANOMATERIALS AND BIOSTRUCTURES, 8 (1), 101-110, 2012, WOS:000316441200011	0,638	8	0,080	0	4	0
8	Edina Rusen, Bogdan Marculescu, Izabela-Cristina Stancu, Ana Maria Albu, C. Grigoras, Dan Sorin Vasilescu- Grafting N-vinyl-carbazole on alternating copolymers obtained from dicyclopentadiene, OPTOELECTRONICS AND ADVANCED MATERIALS, RAPID COMMUNICATIONS, 3 (3), 249-254, 2009, WOS:000265405200020	0,452	6	0,075	0	0	0
9	Florica Adriana Nicolescu, Valentin Victor Jerca, **Izabela-Cristina Stancu,** Dan Sorin Vasilescu, Dumitru Mircea Vuluga- New organic-inorganic hybrids with azo-dye content, DESIGNED MONOMERS AND POLYMERS, 13 (5), 437-444, 2010, WOS:000282736600005	1,528	5	0,306	0	16	0
10	D. M. Dragusin, D. E. Giol, E. Vasile, R. Trusca, M. Teodorescu, **I. Stancu**, D. S. Vasilescu, H. Iovu, Influence of physical interactions on the porosity of gelatin-alginate scaffolds, Optoelectronics and advanced materials – Rapid communications (2011) 5(4), 459 – 464 WOS:000290774800058	0,452	8	0,057	0	0	0
11	Edina Rusen, Bogdan Marculescu, Izabela-Cristina Stancu, C. Grigoras, Dan Sorin Vasilescu- Chemical transformations on copolymers obtained from dicyclopentadiene, MATERIALE PLASTICE, 45 (4), pp: 409-413, 2008, WOS:000262600800020	1,393	5	0,279	0	0	0

12	Adriana Lungu, Madalina G. Albu, **Izabela-Cristina Stancu**, Nicoleta M. Florea, Eugeniu Vasile, Iovu Horia- Superporous collagen-sericin scaffolds, JOURNAL OF APPLIED POLYMER SCIENCE, 127 (3), p:2269-2279, 2013, WOS:000310603100102	2,188	6	0,365	0	26	0
13	Sorina Dinescu, Bianca Galateanu, Eugen Radu, Anca Hermenean, Adriana Lungu, **Izabela-Cristina Stancu**, Dana Jianu, Tudorita Tumbar, Marieta Costache- A 3D Porous Gelatin-Alginate- Based-IPN Acts as an Efficient Promoter of Chondrogenesis from Human Adipose-Derived Stem Cells, STEM CELLS INTERNATIONAL, Article Number: 252909, 17 pg, 2015, WOS:000355851800001	3,902	9	0,434	0	10	0
14	Daniel Chappard, **Izabela-Cristina Stancu-** Porosity imaged by a vector projection algorithm correlates with fractal dimension measured on 3D models obtained by microCT, JOURNAL OF MICROSCOPY, 258 (1), p: 24-30, 2015, WOS:000351381000004	1,813	2	0,907	0	5	0
15	Petre, Daniela; Cecoltan, Sergiu; Serafim, Andrada; Lungu, Adriana; Dragusin, Diana Maria; Stan, Eliza Geta; Tucureanu, Catalin; Vasile, Eugeniu; Salageanu, Aurora; Istodorescu, Mircea; Iovu, Horia; **Stancu, Izabela Cristina**, Composite Particles Gel - Alg - Apatite for Bone Tissue Regeneration, MATERIALE PLASTICE, 53(2) p: 269-272, 2016, WOS:000380629300018	1,393	12	0,116	0	0	0
16	Lisa Terranova, Diana Maria Dragusin, Romain Mallet, Eugeniu Vasile, **Izabela-Cristina Stancu**, Catherine Behets, Daniel Chappard Repair of calvarial bone defects in mice using electrospun polystyrene scaffolds combined with β-TCP or gold nanoparticles, MICRON, 93, p: 29-37, 2017, DOI: 10.1016/j.micron.2016.11.001, WOS:000393017000004	1,530	7	0,219	0	5	0
17	Serafim, Andrada; Constantinescu, Mihai Octavian; Iordache, Florinel Tirdea; Vasile, Eugeniu; Lungu, Adriana; Marinescu, Rodica; **Stancu, Izabela Cristina**, Bio-activation of Inert pHEMA Matrices with Phosphate Loaded Cellulose Fibers in Order to Induce Mineralization, MATERIALE PLASTICE 54(2) p: 235-238, 2017, WOS:000408702100008	1,393	7	0,199	0	0	0

18	Manolescu, Bogdan Stelian Mastalier; Popescu, Valentin; Petrutescu, Marius Septimiu; Serafim, Andrada; **Stancu, Izabela Cristina**, Evaluations of Implanted Polypropylene Mesh After Surgical Removal Due to Eventration or Mesh Rejection, MATERIALE PLASTICE, 54(1), p: 49-52, 2017 WOS:000400629900011	1,393	5	0,279	0	1	0
19	Jerca, Florica Adriana; Anghelache, Alina Maria; Ghibu, Emilian; Cecoltan, Sergiu; **Stancu, Izabela-Cristina**; Trusca, Roxana; Vasile, Eugeniu; Teodorescu, Mircea; Vuluga, Dumitru Mircea; Hoogenboom, Richard; Jerca, Valentin Victor, Poly(2-isopropenyl-2-oxazoline) Hydrogels for Biomedical Applications, CHEMISTRY OF MATERIALS, 30(21) p: 7938-7949, 2018, DOI: 10.1021/acs.chemmater.8b03545, WOS:000450696100061	10,159	12	0,847	0	7	0
20	Cernencu, Alexandra I.; Lungu, Adriana; **Stancu, Izabela-Cristina**; Serafim, Andrada; Heggset, Ellinor; Syverud, Kristin; Iovu, Horia, Bioinspired 3D printable pectin-nanocellulose ink formulations, CARBOHYDRATE POLYMERS, 220, p:12-21, 2019, DOI: 10.1016/j.carbpol.2019.05.026, WOS:000470825500002	6,044	7	0,863	0	6	0
21	Cernencu, Alexandra; Lungu, Adriana; **Stancu, Izabela Cristina**; Vasile, Eugeniu; Iovu, Horia, Polysaccharide-Based 3d Printing Inks Supplemented With Additives, UNIVERSITY POLITEHNICA OF BUCHAREST SCIENTIFIC BULLETIN SERIES B-CHEMISTRY AND MATERIALS SCIENCE, 81(4) p: 175-186, 2019, WOS:000501994100016	0,000	5	0,000	0	0	0
22	Dziadek, Michal ; Douglas, Timothy E. L.; Dziadek, Kinga; Zagrajczuk, Barbara; Serafim, Andrada; **Stancu, Izabela-Cristina**; Cholewa-Kowalska, Katarzyna, Novel whey protein isolate-based highly porous scaffolds modified with therapeutic ion-releasing bioactive glasses, MATERIALS LETTERS, 261, Article Number: 127115, 5 pag, DOI: 10.1016/j.matlet.2019.127115, WOS:000506193100081	3,019	7	0,431	0	0	0

23	Gupta, Dhanak; Kocot, Magdalena; Tryba, Anna Maria; Serafim, Andrada; **Stancu, Izabela C.**; Jaegermann, Zbigniew; Pamula, Elzbieta; Reilly, Gwendolen C.; Douglas, Timothy E. L, Novel naturally derived whey protein isolate and aragonite biocomposite hydrogels have potential for bone regeneration, MATERIALS & DESIGN, 188, 108408, 11 pag, (2020) DOI: 10.1016/j.matdes.2019.108408, WOS:000514567900046	5,770	9	0,641	0	0	0
24	Olaret, Elena ; Ghitman, Jana; Iovu, Horia; Serafim, Andrada; **Stancu, Izabela-Cristina**, Coatings based on mucin-tannic acid assembled multilayers. Influence of pH , POLYMERS FOR ADVANCED TECHNOLOGIES, 31 (4) p: 645-653, 2020, DOI: 10.1002/pat.4783, WOS:000510603300001	2,162	5	0,432	0	0	0
25	Selaru, Aida; Dragusin, Diana-Maria; Olaret, Elena; Serafim, Andrada; Steinmueller-Nethl, Doris; Vasile, Eugeniu; Iovu, Horia; **Stancu, Izabela-Cristina**; Costache, Marieta; Dinescu, Sorina, Fabrication and Biocompatibility Evaluation of Nanodiamonds-Gelatin Electrospun Materials Designed for Prospective Tissue Regeneration Applications, MATERIALS, 12(8), Article Number: 2933, 18 pag, 2019, DOI: 10.3390/ma12182933, WOS:000489126600092	2,972	10	0,297	0		0
	Brevete naționale						
1	Inventatori: **Stancu IC**, Cecoltan S, Petre DG, Lungu A, Serafim A, Drăgușin DM, Vasile E, Marinescu R, Salageanu A, Țucureanu C., Caraș I., Tofan V.C., Istodorescu M. titulari: UPB, Institutul National de cercetare Cantacuzino București, Medical Ortovit SRL *Procedeu de obținere a unor substraturi bionanocompozite hidratate pentru creștere celulară și regenerare/modelare tisulară*, Brevet RO 132544 data eliberării 29.05.2020	1	13	1	-	-	-
			TOTAL	**65,597**	**25**	**490**	**7**

centralizare criterii

	NTOP		FIC	NP	NC	
Izabela-Cristina STANCU	**7**		**65,597**	**25**	**459**	
Criterii CNATDCU - Profesor	***≥4***		***≥30***	***≥20***	***≥120***	Medie
Scor	1,750		2,187	1,25	3,83	2,25

Legenda: NTOP=numar total articole in reviste ISI situate in top 25% (zona rosie) in calitate de autor principal (fie la momentul publicarii fie la data inscrierii la concurs, 10.06.2020) , NP=numar articole autor principal (prim autor sau autor de corespondenta), FIC=factor de impact calculat conform OM6560 (comisia 8); FI = factorul de impact al revistei valabil la 10.06.2020; NC=numar total citari (fara autocitarile candidatului) - din baza Scopus;

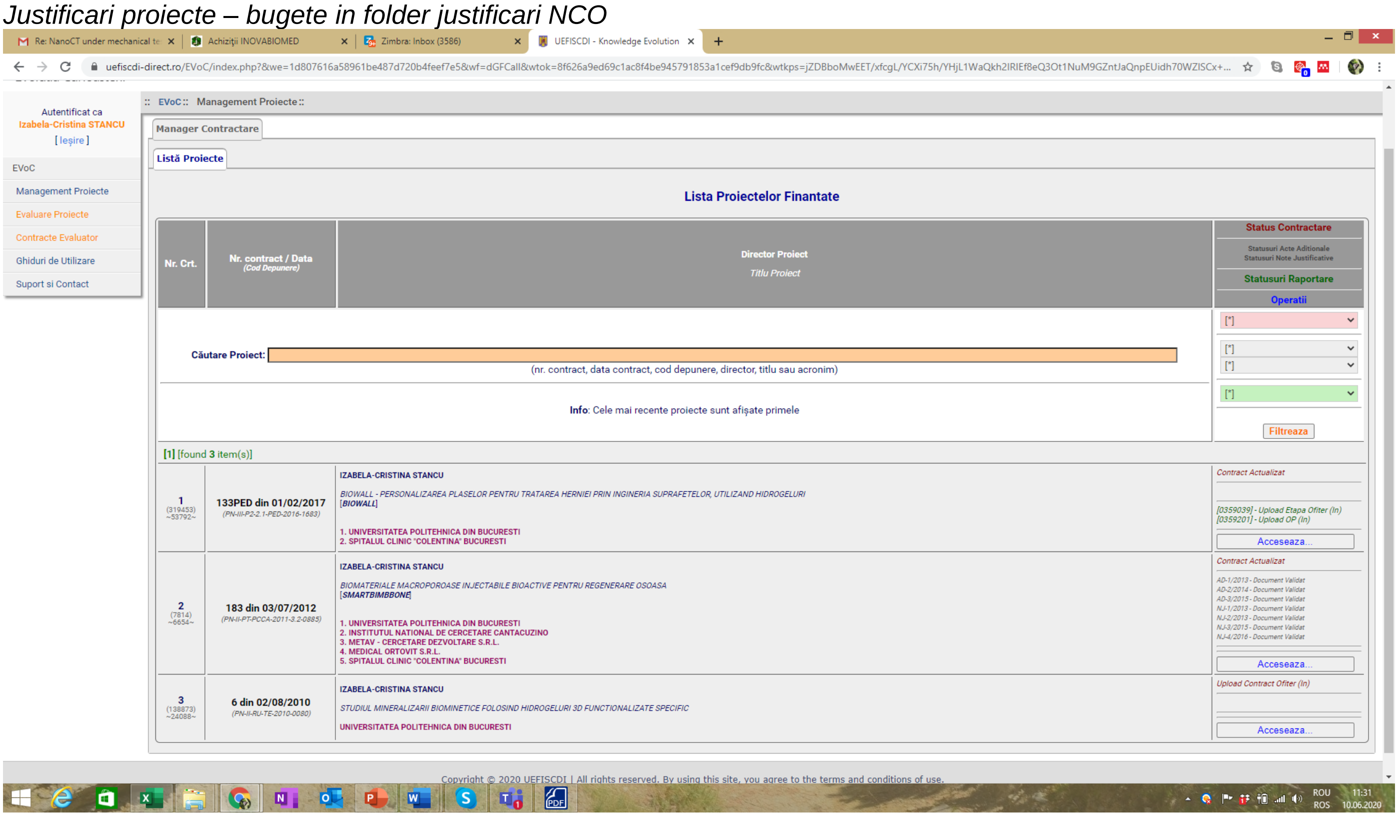
CANDIDAT STANCU IZABELA-CRISTINA
Depart. de Bioresurse şi Ştiinta Polimerilor Fac. de Chimie Aplicată şi Ştiinţa Materialelor

Verificare criteriu NCO , "Stancu, Izabela Cristina" ID SCOPUS 26023804300
TABEL 3b.2. proiecte în calitate de director de proiect

	Proiect câştigat ca DIRECTOR prin competiţie UEFISCDI/CNCSIS	Suma Euro*
1	133PED din 01/02/2017 (PN-III-P2-2.1-PED-2016-1683) BIOWALL - Personalizarea plaselor pentru tratarea herniei prin ingineria suprafetelor, utilizând hidrogeluri [BIOWALL] – 600000 lei	123943
2	183 din 03/07/2012 (PN-II-PT-PCCA-2011-3.2-0885) Biomateriale macroporoase injectabile bioactive pentru regenerare osoasa - 3250000 lei	671362
3	6 din 02/08/2010 (PN-II-RU-TE-2010-0080) Studiul biomineralizarii biomimetice folosind hidrogeluri 3D functionalizate specific - 594440 lei	122795
4	IDEI 729/2009, PCE-2008 Biomateriale polimerice pentru regenerare osoasa. Biomimetism prin nanostructurarea suprafetei - 452498 lei	93473
5	CEEX 5853/18.09.2006, Materiale hibride polimerice performante pentru regenerare osoasa; combinatie revolutionara de biomineralizare sablonata si aderenta celulara - 136000 lei	28093
6	Obtinerea de materiale fibroase de uz ortopedic prin grefare pe suporturi polimerice naturale, Grant AT CNCSIS 2, 175/ 2004) – 5000 lei	1032

estimată la cursul de 1 euro = 4,8409 RON (iunie 2020)
NCO = 5

Justificari proiecte – bugete in folder justificari NCO



CANDIDAT STANCU IZABELA-CRISTINA
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Verificare criteriu NC , "Stancu, Izabela Cristina" ID SCOPUS 26023804300

TABEL 3b.3. Lucrarea citată însoţită de citările din baza Scopus

1	**Lucrare citată:** Cernencu, Alexandra I.; Lungu, Adriana; **Stancu, Izabela-Cristina**; Serafim, Andrada; Heggset, Ellinor; Syverud, Kristin; Iovu, Horia, Bioinspired 3D printable pectin-nanocellulose ink formulations, **CARBOHYDRATE POLYMERS**, 220, 12-21, 2019, DOI: 10.1016/j.carbpol.2019.05.026, WOS:000470825500002 6 citări fără autocitările candidatei
	1. Cargnin, M.A., de Souza, A.G., de Lima, G.F., Gasparin, B.C., Rosa, D.D.S., Paulino, A.T. Pinus residue/pectin-based composite hydrogels for the immobilization of β-D-galactosidase (2020) 149, pp. 773-782, EID 2-s2.0-85078924728 2. Rincón-Iglesias, M., Delgado, A., Peřinka, N., Lizundia, E., Lanceros-Méndez, S., Water-based 2D printing of magnetically active cellulose derivative nanocomposites, (2020) 233, art. no. 115855, EID 2-s2.0-85077675036 3. Vlasceanu, G.M., Crica, L.E., Pandele, A.M., Ionita, M. Graphene oxide reinforcing genipin crosslinked chitosan-gelatin blend films, (2020) 10 (2), art. no. 189, EID 2-s2.0-85080870467 4. Ferreira, F.V., Otoni, C.G., De France, K.J., Barud, H.S., Lona, L.M.F., Cranston, E.D., Rojas, O.J., Porous nanocellulose gels and foams: Breakthrough status in the development of scaffolds for tissue engineering (2020) EID 2-s2.0-85082798852 5. Fiorati, A., Negrini, N.C., Baschenis, E., Altomare, L., Faré, S., Schieroni, A.G., Piovani, D., Mendichi, R., Ferro, M., Castiglione, F., Mele, A., Punta, C., Melone, L., TEMPO-nanocellulose/Ca2+ hydrogels: Ibuprofen drug diffusion and in vitro cytocompatibility (2020) 13 (1), p. 183, EID 2-s2.0-85079735827 6. Luo, H., Cha, R., Li, J., Hao, W., Zhang, Y., Zhou, F., Advances in tissue engineering of nanocellulose-based scaffolds: A review, (2019) 224, art. no. 115144, EID 2-s2.0-85070077483
2	**Lucrare citată:** Degeratu, C.N., Mabilleau, G., Aguado, E., Mallet, R., Chappard, D., Cincu, C., **Stancu, I.C**., Polyhydroxyalkanoate (PHBV)fibers obtained by a wet spinning method: Good in vitro cytocompatibility but absence of in vivo biocompatibility when used as a bone graft | [Fibres de polyhydroxyalkanoate (PHBV)obtenues par une méthode de filage humide: bonne cytocompatibilité in vitro mais absence de biocompatibilité in vivo en site osseux], **MORPHOLOGIE** 103(341), pp. 94-102, 2019 3 citări fără autocitările candidatei
	1. Wang, J., Tan, H., Li, K., Yin, H. Two-stage fermentation optimization for poly-3-hydroxybutyrate production from methanol by a new Methylobacterium isolate from oil fields (2020) 128 (1), pp. 171-181, EID 2-s2.0-85074246098 2. She, R., Zhang, Y., Chen, L., Wang, Y., Zhang, B., Huang, Q., Biocompatibility of tissue engineered cartilage constructedin vivoby silk fibroin-chitosan scaffold carrying bone marrow mesenchymal stem cells (2020) 24 (1), art. no. 2095-4344(2020)01-00027-06, pp. 27-32, EID 2-s2.0-85078292859 **3.** Grigore, M.E., Grigorescu, R.M., Iancu, L., Ion, R.-M., Zaharia, C., Andrei, E.R. Methods of synthesis, properties and biomedical applications of polyhydroxyalkanoates: a review (2019) 30 (9), pp. 695-712. EID 2-s2.0-85064815890
3	**Lucrare citată:** Jerca, Florica Adriana; Anghelache, Alina Maria; Ghibu, Emilian; Cecoltan, Sergiu; **Stancu, Izabela-Cristina**; Trusca, Roxana; Vasile, Eugeniu; Teodorescu, Mircea; Vuluga, Dumitru Mircea; Hoogenboom, Richard; Jerca, Valentin Victor, Poly(2-isopropenyl-2-oxazoline) Hydrogels for Biomedical Applications, **CHEMISTRY OF MATERIALS**, 30(21): 7938-7949, 2018, DOI: 10.1021/acs.chemmater.8b03545, WOS:000450696100061 7 citări fără autocitările candidatei
	1. Douglas, T.E.L., Keppler, J.K., Vandrovcová, M., Plencner, M., Beranová, J., Feuereisen, M., Parakhonskiy, B.V., Svenskaya, Y., Atkin, V., Ivanova, A., Ricquier, P., Balcaen, L., Vanhaecke, F., Schieber, A., Bačáková, L., Skirtach, A.G., Enhancement of biomimetic enzymatic mineralization of gellan gum polysaccharide hydrogels by plant-derived gallotannins (2020) 21 (7), art. no. 2315, EID 2-s2.0-85082791589 2. Raus, V., Hološ, A., Kronek, J., Mosnáček, J. Well-Defined Linear and Grafted Poly(2-isopropenyl-2-oxazoline)s Prepared via Copper-Mediated Reversible-Deactivation Radical Polymerization Methods (2020) 53 (6), pp. 2077-2087, EID 2-s2.0-85082335186 3. Amirova, A., Rodchenko, S., Kurlykin, M., Tenkovtsev, A., Krasnou, I., Krumme, A., Filippov, A. Synthesis and investigation of thermo-induced gelation of partially cross-linked poly-2-isopropyl-2-oxazoline in aqueous media (2020) 12 (3), art. no. 698, EID 2-s2.0-85082719170 4. Sun, X., Luo, C., Luo, F. Preparation and properties of self-healable and conductive PVA-agar hydrogel with ultra-high mechanical strength (2020) 124, art. no. 109465, EID 2-s2.0-85077234691 5. Xu, X., Jerca, F.A., Van Hecke, K., Jerca, V.V., Hoogenboom, R. High compression strength single network hydrogels with pillar[5]arene junction points (2020) 7 (2), pp. 566-573, EID 2-s2.0-85079510048 6. Spicer, C.D. Hydrogel scaffolds for tissue engineering: The importance of polymer choice (2020) 11 (2), pp. 184-219. 2-s2.0-85077545378

	7. Xu, X., Jerca, F.A., Jerca, V.V., Hoogenboom, R. Covalent Poly(2-Isopropenyl-2-Oxazoline) Hydrogels with Ultrahigh Mechanical Strength and Toughness through Secondary Terpyridine Metal-Coordination Crosslinks (2019) 29 (48), art. no. 1904886, EID 2-s2.0-85073932132
4	**Lucrare citată:** Serafim, Andrada; Olaret, Elena; Cecoltan, Sergiu; Butac, Livia Maria; Balanuca, Brindusa; Vasile, Eugeniu; Ghica, Mihaela; **Stancu, Izabela Cristina**, Bicomponent Hydrogels Based on Methacryloyl Derivatives of Gelatin and Mucin with Potential Wound Dressing Applications, **MATERIALE PLASTICE**, 55(1): 68-74, 2018 WOS:000444129500015 3 citări fără autocitările candidatei
	1. Dobrota, D. Corrosion of welded metal structures of mining equipment (2018) Revista de Chimie, 69 (9), pp. 2563-2566. EID 2-s2.0-85054335114 2. Petrou, G., Crouzier, T. Mucins as multifunctional building blocks of biomaterials (2018) Biomaterials Science, 6 (9), pp. 2282-2297. EID 2-s2.0-85052118759 3. Radu, I.C., Vasile, E., Damian, C.M., Iovu, H., Stanescu, P.O., Zaharia, C. Influence of the double bond LDH clay on the exfoliation / intercalation mechanism of polyacrylamide nanocomposite hydrogels (2018) Materiale Plastice, 55 (3), pp. 263-268. EID 2-s2.0-85055354916
5	**Lucrare citată:** Cecoltan, Sergiu; **Stancu, Izabela-Cristina**; Dragusin, Diana Maria; Serafim, Andrada; Lungu, Adriana; Tucureanu, Catalin; Caras, Iuliana; Tofan, Vlad Constantin; Salageanu, Aurora; Vasile, Eugeniu; Mallet, Romain; Chappard, Daniel; Coman, Cristin; Istodorescu, Mircea; Iovu, Horia, Nanocomposite particles with improved microstructure for 3D culture systems and bone regeneration, JOURNAL OF MATERIALS SCIENCE-MATERIALS IN MEDICINE, 28(10), Article Number: 153, 2017, DOI: 10.1007/s10856-017-5966-8, WOS:000411111500009 2 citări fără autocitările candidatei
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7	**Lucrare citată:** Manolescu, Bogdan Stelian Mastalier; Popescu, Valentin; Petrutescu, Marius Septimiu; Serafim, Andrada; **Stancu, Izabela Cristina**, Evaluations of Implanted Polypropylene Mesh After Surgical Removal Due to Eventration or Mesh Rejection, MATERIALE PLASTICE, 54(1), 49-52, 2017 WOS:000400629900011 1 citări fără autocitările candidatei
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8	**Lucrare citată:** Lisa Terranova, Diana Maria Dragusin, Romain Mallet, Eugeniu Vasile, **Izabela-Cristina Stancu**, Catherine Behets, Daniel Chappard Repair of calvarial bone defects in mice using electrospun polystyrene scaffolds combined with β-TCP or gold nanoparticles, MICRON, 93, 29-37, 2017, DOI: 10.1016/j.micron.2016.11.001, WOS:000393017000004 5citări fără autocitările candidatei
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	3. Dantas, A., Valério, A., Ninow, J.L., de Oliveira, J.V., de Oliveira, D. Potential application of Thermomyces lanuginosus lipase (TLL) immobilized on nonporous polystyrene particles (2019) Environmental Progress and Sustainable Energy, 38 (2), pp. 608-613. EID 2-s2.0-85053670644 4. Strub, M., Van Bellinghen, X., Fioretti, F., Bornert, F., Benkirane-Jessel, N., Idoux-Gillet, Y., Kuchler-Bopp, S., Clauss, F. Maxillary Bone Regeneration Based on Nanoreservoirs Functionalized ϵ -Polycaprolactone Biomembranes in a Mouse Model of Jaw Bone Lesion (2018) BioMed Research International, 2018, art. no. 7380389, EID 2-s2.0-85044157801 5. Tamburaci, S., Tihminlioglu, F. Novel poss reinforced chitosan composite membranes for guided bone tissue regeneration (2018) Journal of Materials Science: Materials in Medicine, 29 (1), art. no. 1, EID 2-s2.0-85037349177
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10	**Lucrare citată:** Serafim, A., Draguşin, D.-M., Butac, L.M, Vasilescu, D.S., Dubruel, P., **Stancu, I.-C**. New hydrogels based on gelatin and acrylamide, UPB Scientific Bulletin, Series B: Chemistry and Materials Science 75(2), pp. 3-14, 2013, ISSN 1454-2331. 1 citări fără autocitările candidatei
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11	**Lucrare citată:** Andrada Serafim, Sergiu Cecoltan, Adriana Lungu, Eugeniu Vasile, Horia Iovu, **Izabela-Cristina Stancu** - Electrospun fish gelatin fibrous scaffolds with improved bio-interactions due to carboxylated nanodiamond loading, RSC ADVANCES, ISSN: 2046-2069, 5 (116), 95467, 2015, DOI: 10.1039/c5ra14361f (WOS:000364907300009), EID: 2-s2.0-84947093650, Article 5 citări fără autocitările candidatei
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	NC
Criterii CNATDCU – Profesor (in total in baza SCOPUS)	***≥120***
Izabela-Cristina STANCU	**490**

Justificare Tabel 3b.1 – referitor calitate autor de corespondenta al lucrarilor:
Andrada Serafim, Sergiu Cecoltan, Adriana Lungu, Eugeniu Vasile, Horia Iovu, ***Stancu I.C.***
Electrospun fish gelatin fibrous scaffolds with improved bio-interactions due to carboxylated nanodiamond loading
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RSC Advances

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PAPER

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Electrospun fish gelatin fibrous scaffolds with improved bio-interactions due to carboxylated nanodiamond loading

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Nanotechnology and biomimicry represent appealing but still underexploited techniques to develop innovative scaffolds with ECM-inspired features for tissue engineering. In the present work we have investigated the potential of a combination of two designed elements to trigger enhanced bio-interactions with bone regeneration potential: COOH-functionalized nanodiamond particles (COOH-NDPs) have been loaded for the first time into electrospun fish gelatin hydrogel fibers thus generating nanocomposite fibrous scaffolds with interconnected porosity. When compared to control fish gelatin fibers, no significant modification of the mineralization capacity in acellular simulated body fluid has been evidenced by micro-structural and spectroscopic investigations, for fibers with COOH-NDPs content ranging from 0.25% to 1%. It is important to mention that, following Ca/P alternate incubation, nano-apatite crystals were preferentially developed and firmly adhered on the fiber regions in the proximity of COOH-NDPs, as proven by transmission electron microscopy (TEM). Significant mineralization occurred in the culture media in the presence of MG63 osteoblast-like cells and seems to be directly stimulated by the presence of the nanoparticles. Altogether, these findings emphasize the ability of NDPs to enhance, when immobilized in gelatin fibers and exposed to specific media, the formation of apatite. It was also noticed that the number of adherent MG63 cells, their morphology and spreading were improved by increasing the amount of NDPs in the fibers (fluorescence and scanning electron microscopy). This work successfully proves the potential of such nanocomposite fibers to find applications in bone regeneration.

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Introduction

While tissue engineering allows the design of biological substitutes to repair or replace damaged organs or tissues, nanotechnology related research provides the means for mimicking the morphologic features of the extracellular matrix (ECM). The use of nanostructures in combination with polymer matrices has become an appealing approach to improve the performances of a scaffold. The high surface to volume ratios of nanoparticles is responsible for a number of improved behaviors such as increased capacity to interact with the host matrix, enhanced ability to adsorb cell adhesion proteins or other biologically-relevant species, as well as higher mechanical properties. Nanocomposites are multiphase materials containing at least one type of nanostructures. One of the most intensively studied natural nanocomposites is the ECM of hard tissues. Its extraordinary mechanical strength may be attributed to the composition and intimate interaction between its main constituents: nano-apatite as inorganic phase and collagen fibrils within the hydrogel matrix. The modern design of biomaterials for scaffold-assisted bone regeneration often starts with an approach inspired by this nanocomposite. The development of nanostructured composite scaffolds based on biomimetic nanoparticles and hydrogels appears as a promising route for mimicking the natural environment of cells. Whereas nano-apatite/hydrogel composites are widely explored in this aim,[1] the development of nanocomposites based on nanodiamond particles (NDPs) and hydrogels recently gained increased attention. NDPs are biomimetic nanostructures demonstrating, in addition to excellent mechanical properties and chemical inertness, higher biocompatibility when compared to other carbon-based species such as carbon black, single- and multi-walled carbon nanotubes (SWNTs, MWNTs).[2,3] Only limited research describe NDPs-reinforced apatite coatings and films developed for medical metal materials[4,5] or composites with biomineralization ability, based on NDPs and biodegradable polymers.[6,7] Despite the potential of these

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Research Article

Osteoblast-Like Cell Behavior on Porous Scaffolds Based on Poly(styrene) Fibers

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Scaffolds of nonresorbable biomaterials can represent an interesting alternative for replacing large bone defects in some particular clinical cases with massive bone loss. Poly(styrene) microfibers were prepared by a dry spinning method. They were partially melted to provide 3D porous scaffolds. The quality of the material was assessed by Raman spectroscopy. Surface roughness was determined by atomic force microscopy and vertical interference microscopy. Saos-2 osteoblast-like cells were seeded on the surface of the fibers and left to proliferate. Cell morphology, evaluated by scanning electron microscopy, revealed that they can spread and elongate on the rough microfiber surface. Porous 3D scaffolds made of nonresorbable poly(styrene) fibers are cytocompatible biomaterials mimicking allogenic bone trabeculae and allowing the growth and development of osteoblast-like cells *in vitro*.

1. Introduction

The increasing frequencies of traumatic and pathologic bone defects, as well as the skeletal problems due to osteoporosis and bone degeneration in aging population, request a societal need for improved therapeutic products. The need for biomimetic scaffold materials as alternative to bone auto- or allografts is well recognized [1]. Consequently, the investigation of artificial materials for bone repair remains a constant key concern in the field of biomaterials research for clinical applications. It is widely accepted that three-dimensional porous constructs are needed to lodge bone cells and to provide the template for tissue formation and development, including angiogenesis. Synthetic or natural ceramics are either too brittle to be used in weight-bearing bones (e.g., β-Tri calcium phosphate) or massive and impossible to resorb by bone remodeling (e.g., coral or hydroxyapatite blocks). Biodegradable biocompatible polymers have been proposed to fill small bone defects. Clinical situations exist where large bone defects cannot be replaced by such resorbable materials which also present important drawbacks (e.g., polylactic or polyglycolic acid) [2, 3]. Large bone flaps of the skull are done in neurosurgery for the treatment of tumors or large pelvic amputations occurring in the case of sarcoma or metastasis. Reconstruction with a variety of nonresorbable materials has been proposed (tantalum or titanium plates, PMMA plates prepared with bone cement...) but none has been found satisfactory [4]. For example, PMMA is biotolerated and always encapsulated by a thin layer of fibrosis. Unlike biodegradable macromolecules, nonbiodegradable and biocompatible polymers such as polyhydroxyethyl methacrylate and poly(styrene) could represent interesting solutions to generate permanent scaffolds supporting bone regeneration in case of extensive bone losses. We have investigated polyhydroxyethyl methacrylate as an interesting synthetic hydrogel for bone biomaterials [5–8]. However, its use in load bearing applications may be limited by insufficient mechanical strength in hydrated form. Therefore, we considered

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One-pot synthesis of superabsorbent hybrid hydrogels based on methacrylamide gelatin and polyacrylamide. Effortless control of hydrogel properties through composition design

Andrada Serafim,†[a] Catalin Tucureanu,†[b] Daniela-Geta Petre,[a] Diana-Maria Dragusin,[c] Aurora Salageanu,[b] Sandra Van Vlierberghe,[c] Peter Dubruel[c] and Izabela-Cristina Stancu*[a]

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Biocompatible methacrylamide-modified gelatin (GELMA) hydrogels with tuned characteristics, obtained through network-forming photopolymerization, have recently attracted increasing attention due to their wide range of possible applications such as drug release, tissue regeneration and generation of bioartificial implants. Due to the controlled number of C═C bonds, GELMA may simultaneously act as macromonomer and crosslinker leading through polymerization to hydrogels with rationally designed performances. This study provides effortless one-pot synthesis of hybrid hydrogels based on covalently linked GELMA and polyacrylamide (PAA), using photo-induced network-forming polymerization. Conventional synthesis of similar hydrogels leads to interpenetrating gelatin and PAA networks, usually involving multistep crosslinking of the components and the use of toxic crosslinkers. Through the described one-pot chemistry, the synthetic water superabsorbent PAA with its well-recognized advantages can rationally benefit from the high biocompatibility and cell-adherence of GELMA in a simple covalent way. This work provides a correlation between the composition and the corresponding hydrogel properties (including swelling, pH influence, mechanical behaviour, ability to generate porous scaffolds, enzymatic degradation). The addition of PAA modulated the network density and the water affinity allowing the control of elasticity and degradability. Supplementary crosslinking of the synthetic component provided additional control over hydrophilicity. The capacity of such hydrogels to generate porous scaffolds was proved; interesting morphologies were developed only by varying the composition. *In vitro* cellular studies indicated that the presence of GELMA conferred controlled cell-affinity properties to the bicomponent hydrogels. Nevertheless, the drug release potential of such hydrogels was preliminarily investigated using sodium nafcillin. GELMA–PAA hydrogels may be useful for tissue regeneration due to effortless synthesis, compositional flexibility and variable properties.

1. Introduction

Hydrogels are hydrophilic polymers with an intrinsic three-dimensional (3D) structure extensively studied as biomaterials due to their mechanical, physico-chemical and functional resemblance with the extracellular matrix (ECM). These materials are water insoluble, soft and elastic when hydrated, and represent interesting scaffolds for tissue engineering, cell encapsulation and drug delivery applications. Van Vlierberghe *et al.* recently reviewed key aspects related to biopolymer-based hydrogels with applications in tissue engineering.[1] Unlike natural hydrogels, synthetic counterparts present as main advantage the possibility to control their composition, polymerization, degradation, mechanical behaviour and even biocompatibility. Accordingly, synthetic hydrogels can be, from a chemical point of view, better defined and developed with a panel of selected properties adapted to provide the best outcome with respect to key characteristics of the ECM.[2] Furthermore, it is recognized that synthetic hydrogels reduce the variability between *in vitro* studies and decrease the potential immunorejection.[2] However, their lack of biological cues and cell recognition features justify the need to further combine

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† The contribution of Andrada Serafim is the synthesis and characterization of the materials. Catalin Tucureanu performed the biological characterization.

Serafim, A., Vasile E., Iovu H, ***Stancu I.C.***
Self-assembled gold-dendrimer composite nanoparticles as surface nanostructuring features
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SELF-ASSEMBLED GOLD-DENDRIMER COMPOSITE NANOPARTICLES AS SURFACE NANOSTRUCTURING FEATURES

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Various gold-dendrimer nanocomposites were obtained through a simple colloidal chemistry method, using two types of carboxyl-terminated dendrimers, without additional reducing agents, at room temperature. Polyamidoamine dendrimers with simple carboxyl ending groups and with a short tetrafunctional ethylenediamine core have been used, as well as polyamidoamine dendrimers with succinamic acid terminal groups and dodecanediamine tetrafunctional core. The concentration of carboxyl ending groups has been maintained constant, at values of 1mM and, respectively 2mM. Gold nanoparticles obtained using sodium citrate at the same concentration of COO- have been synthesized and used as control. All the so-formed particles were used to generate nanostructured coatings for various substrates.

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Keywords: Gold-dendrimer nanocomposite; PAMAM; Nanoparticles; Nanostructured coating

1. Introduction

Recently there is an increasing interest and awareness of the use of noble metal nanoparticles in various applications such as sensors, drug delivery and advanced medical applications [1-10]. Various methods of colloidal chemistry have been elaborated for obtaining noble metal nanoparticles, including the use of plant extracts [11-12]. We recently synthesized gold nanoparticles using a citrate-mediated reduction, in order to induce the biomimetic calcification (formation of bone-like apatite) on different substrates, after surface coating with carboxyl-ended self assembled monolayers [2]. Accordingly, the surface of poly(2-hydroxyethyl methacrylate) (PHEMA) has been nanostructured using gold nanoparticles modified with a carboxyl-ended thiol. The so-formed spherical beads have been used to homogeneously coat the polymer surface, leading to a nanostructured topography. In the present study we evaluated the possibility to further use gold nanoparticles in order to nanostructure surfaces obtaining different topographies. Noble metals-dendrimer composite nanoparticles have been obtained in the last 15 years in the presence of dendrimers through already common procedures [1, 13-23]. Dendrimers are well known globular macromolecules with a typical architecture with branches diverging from a central core; the multifunctionality and the monodispersity are among their most important specific features. Therefore, these molecules represent interesting hosts to accommodate, initiate and further guide crystal development inside the internal cages of their tree-like skeleton. Different factors such as the dendrimer type, chemistry, generation number, terminal and internal chemical

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RESEARCH PAPER

Apatite formation on active nanostructured coating based on functionalized gold nanoparticles

Eugeniu Vasile · Andrada Serafim · Diana-Maria Dragusin · Celina Petrea · Horia Iovu · Izabela-Cristina Stancu

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Abstract In this work, we developed a simple method of surface functionalization of polymer substrates to provide them with the ability to form biomimetic hydroxyapatite (HA) when incubated in synthetic body fluids (SBF). In a first step, gold nanoparticles (AuNPs) were used as surface nanostructuring units for a biocompatible polymer, poly(2-hydroxyethyl methacrylate), known to not promote biomineralization in SBF, and under physiological conditions. The treatment of AuNPs-modified substrate with mercaptosuccinic acid leads to brushes of carboxyl-ended chains self-assembled onto the gold-polymer hybrid nanosurface. The main aim of this work was to demonstrate that these multianionic nanosurfaces would induce HA formation when incubated in solutions mimicking physiologic conditions. The formation of apatite and its morphology and composition were successfully investigated by means of high resolution scanning and transmission electron microscopy with energy dispersive X-ray microanalysis, infrared spectroscopy, X-ray photoelectron spectroscopy, and X-ray diffraction. Emphasis was put on the nucleation of HA in areas with agglomerated carboxyl-ended functionalized nanoparticles. The results obtained in this study may unlock new applications for smart active coatings based on functionalized AuNPs, such as the induction of biomineralization.

Keywords Gold nanoparticles · Apatite · Biomineralization · Thin layer

Introduction

Metallic nanoparticles have recently gained important development in a wide range of applications due to their special optical and electronic properties as well as due to their morphology-related characteristics. Gold nanoparticles (AuNPs) are extensively researched for nanotechnology uses including advanced medical treatment. The small size and high surface-to-volume ratio, together with the easy modification through various functional self-assembled monolayers (SAMs) by thiol-mediated methods, make them ideal candidates for applications requiring multifunctional and nanostructured surfaces. Therefore, in the present study, we used AuNPs decorated with carboxyl-ended SAMs to nanostructure the surface of a polymer in the aim of providing the substrate with biomineralization (formation of bone-like apatite) potential.

The current trends in the design of biomaterials for bone engineering are based on structure–properties relationship. It is widely accepted that hydroxyapatite

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Chemoselective cross-linking of alginate with thiol-terminated peptides for tissue engineering applications

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Chemoselective cross-linking of alginate with thiol-terminated peptides for tissue engineering applications

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ABSTRACT

In this study we chemospecifically functionalized alginate with thiol-ended peptides for tissue engineering (TE); a carbodiimide linker and the disulfide exchange scheme were used. First carboxyls of alginate were activated by introducing N-hydroxysuccinimide (NHS) ester groups; these react with primary amines of the heterobifunctional reagent 2-(2-pyridyldithio)ethyleneamine (PDEA). Thiol-reactive alginate (alginate-S-S-py) forms as cross-linking intermediate. The degree of pyridyldithio-functionalization is modified through variable PDEA concentration and it was determined using UV–VIS spectroscopy and proton nuclear magnetic resonance. The applicability of the alginate-S-S-py as platform for the chemoselective coupling of thiol-ended peptides was tested with glutathione as model peptide. Other SH-terminal peptides were successfully cross-linked. Moreover, the peptide–alginate keeps its gel-forming ability when treated with Ca^{2+} cations, leading to functionalized hydrogels that can be further used to obtain different multicomponent systems. The developed chemoselective strategy of functionalizing alginate with thiol-ended peptides could enhance the potential of this polymer for TE.

1. Introduction

Alginates are widely used in tissue engineering (TE) applications ranging from bulking agents, drug delivery systems, cells carrier, and model extracellular matrix (ECM) (for review see: Alexander, Hyun, & David, 2006; Lee & Mooney, 2012).

This polysaccharide belongs to the family of unbranched binary copolymers containing 1–4 glycosidically-linked β-D-mannuronic acid (M) and its C-5 epimer, α-L-guluronic acid (G). Sodium alginate is extracted with a diluted alkali solution from brown algae and is not a random polysaccharide; depending on the algae source, it consists of blocks of similar and strictly alternating residues (i.e. M-blocks, G-blocks, and GM-blocks) (for details see review in Moe, Draget, Skjåk-Bræk, & Smidsrød, 1995). Sodium alginate is soluble in aqueous solutions and forms stable gels at room temperature in the presence of non-cytotoxic concentrations of certain bivalent cations (i.e. Ba^{2+}, Ca^{2+}) through ionic interaction with G groups. This enables hydrogels to be formed, often with viable cells embedded in the gel by cross-linking in non-cytotoxic conditions (Klöck et al., 1997). Advantageous properties like high biocompatibility and nonimmunogenicity made alginate suitable as biomaterial (Shapiro & Cohen, 1997). However, this polysaccharide is unable to specifically interact with mammalian cells (Smetana Jr, 1993). It is widely admitted that cell adhesion can be promoted by decoration of the polymer backbone with cellular adhesion species (Alexander et al., 2006; Rowley, Madlambayan, & Mooney, 1999). On the other hand it is generally accepted that short aminoacid sequences successfully mediate cellular events. A common example consists in the use of arginine glycine aspartic acid (RGD) sequence and its subtypes to promote cell adhesion (Kreeger, Woodruff, & Shea, 2003; Rowley et al., 1999; Simmons, Alsberg, Hsiong, Kim, & Mooney, 2004). It is unlikely that materials modified only with the ubiquitous linear RGD signal will lead to controlled responses of a specific cell type in complex environments (e.g. in vivo) (Healy, 1999). Consequently, other adhesive peptides that can be recognized by the cell membrane need to be used for the design of biomimetic materials for TE. In this context, another amino acid sequence used as heparin binding domain, Lys-Arg-Ser-Arg (KRSR), was demonstrated to enhance osteoblast specific attachment after 4 h while no significant attachment of endothelial cells and fibroblasts was

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Dragusin D.M., Van Vlierberghe S, Dubruel P, Dierick M, Van Hoorebeke L, H. A Declercq, M. M Cornelissen, ***Stancu I.C.***
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PAPER

Novel gelatin–PHEMA porous scaffolds for tissue engineering applications

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In the present work, novel bicomponent polymeric hydrogels based on methacrylamide-modified gelatin (MAG) and 2-hydroxyethyl methacrylate (HEMA) have been prepared by cross-linking polymerization using photoinitiation. Five types of novel hydrogels have been prepared using different MAG/HEMA ratios between 1/0.5 and 1/10 w/w. Subsequently, porous scaffolds were obtained *via* a cryogenic treatment followed by freeze-drying. Physico-chemical measurements as well as *in vitro* degradation tests have been performed in order to correlate the material composition with the corresponding properties. Among the properties studied we have to mention the water uptake capacity, the rheological properties and the enzyme-mediated degradation behaviour. The results indicate that the HEMA content in the initial polymerization mixtures modulates the architecture of the porous scaffolds from straightforward, top-to-bottom oriented channels for hydrogels possessing the lowest HEMA content to a complex and dense internal porosity of the channels the case of higher HEMA loaded materials. While aiming at tissue engineering applications, it is important to notice that the covalently bound gelatin sequences significantly improve the biocompatibility of PHEMA based hydrogels.

1. Introduction

Hydrogel science has developed extensively over time since 1960 when the first usage of poly(2-hydroxyethyl methacrylate) (PHEMA) as a cross-linked hydrophilic network for contact lens fabrication was reported.[1] In 2000, Peppas defined the term *hydrogel* as "three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids." Accordingly, "the networks are composed of homopolymers or copolymers, and are insoluble due to the presence of chemical or physical crosslinks."[2]

Hydrogels based on natural or synthetic (co)polymers are considered suitable for tissue engineering (TE) and regenerative medicine. Moreover, hydrogels consisting of two or more components represent reliable materials for TE applications due to the superior properties of the final product when compared with the properties of each individual component. Gelatin is one of the most investigated natural products used for such a purpose; this protein has been intensively studied for biomaterials applications[1,3–10] due to its collagenic nature, biocompatibility, relatively simple processing ability, temperature-sensitivity, and, last but not least, low cost. Methacrylamide-modified gelatin (MAG) has been recently developed and investigated for tissue regeneration purposes including wound treatment and attachment and growth of a wide variety of human cells.[11–17] This material is obtained through the direct reaction of primary amines from gelatin and methacrylic anhydride[14] and it can present various substitution degrees (DS). MAG's main advantage when compared to unmodified gelatin consists of the possibility of chemical crosslinking by the photoinitiated polymerization of C=C bonds.

On the other hand, 2-hydroxyethyl methacrylate (HEMA) is an important synthetic monomer used to manufacture soft contact lenses and intraocular lenses.[1,18] HEMA-based materials are also applied as embedding substrates for the examination of cells using light microscopy, inert matrices for the slow release of drugs[19,20] and synthetic dural prosthesis.[21] It is also well-known that PHEMA does not allow cell adhesion and proliferation on its surface. As an immediate consequence its biomedical applications are limited when cell cohesion is required. Several methods for PHEMA modification that improve the biological response of the polymer have been already reported in the literature.[22–24] HEMA-based (co)polymers present high biocompatibility and excellent blood compatibility.[25–27] PHEMA is a hydrophilic polymer and exhibits a relatively high degree of hydration (up to 42% of water can be absorbed per mass unit of lightly cross-linked PHEMA).[28]

In the present study, we aimed at the development of novel bicomponent polymer materials based on chemically combined MAG and HEMA. Photoinitiation was used to simultaneously

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Dragusin D. M., Giol D. E., Serafim A., Vasile, E., Zecheru, T., ***Stancu, I. C.***

Casein - PHEMA: In vitro formation of nanometric Ca-P nuclei

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CASEIN – PHEMA: *IN VITRO* FORMATION OF NANOMETRic Ca-P NUCLEI

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This work reports the synthesis of polymeric hybrids based on Casein and 2-hydroxyethyl methacrylate polymers (PHEMA). Protein physical immobilization during the free-radical polymerization was performed. Two strategies were used to generate both films and cylinders. The homogeneity and the stability of the hybrids were assessed as well as their capacity to perform *in vitro* calcification when incubated in synthetic human plasma (SBF) for 14 days. Nucleation islets of calcium phosphate mineral in the form of nanometric nodules (20-30 nm) were observed on the Cas-rich domains. This study reports for the first time the synthesis of Cas-PHEMA materials and it tried to determine if these hybrids could cause a calcification under *in vitro* conditions.

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Keywords: PHEMA, Casein, hybrid, calcification

1. Introduction

Casein (Cas) represents the main protein of milk and its potential in delivering micronutrients has recently regained attention [1-3]. Cas is one of the most extensively studied proteins from the point of view of its structure and functions. Livney [1] has emphasized the fact that this phosphoprotein has a recognized role in providing bioactive nutrients such as calcium and phosphate [1-3]. The affinity of Cas phosphopeptides (CPP) towards calcium and amorphous calcium phosphate (ACP) is well recognized [1,4,5]. CPP are bioactive peptides that can be obtained from by the enzymatic hydrolysis of Cas. The ability of Cas to bind metallic ions (including calcium) is associated to the phosphor-seryl moieties [6-8] flanked by glutamate residues [3,6,8]. The anticariogenic properties of CPP-ACP nano-complexes are reported in several studies [9-13]. In a different work, Wong and Sissons studied the influence of Cas as macronutrient on the calcium phosphate deposition and growth in plaque mineralisation [14]. To our knowledge, despite the well recognised relationship between dietary proteins like Cas and bone quality/density, there are no studies investigating the spontaneous mineralisation ability of Cas when immobilised in polymer carriers. In this context, the present work tried to determine if apatite nucleation occurs *in vitro* on Cas-polymer organic hybrids when poly(2-hydroxyethyl methacrylate) (PHEMA) was selected as a biocompatible carrier.

2. Materials and Methods

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Poly(2-hydroxyethyl methacrylate-co-dodecyl methacrylate-co-acrylic acid): synthesis, physico-chemical characterisation and nafcillin carrier

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Poly(2-hydroxyethyl methacrylate-co-dodecyl methacrylate-co-acrylic acid): synthesis, physico-chemical characterisation and nafcillin carrier

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Abstract In the present study polymeric microbeads of poly(2-hydroxyethyl methacrylate-co-dodecyl methacrylate-co-acrylic acid) or p(HEMA-co-dDMA-co-AA) were synthesised and characterized through FT-IR and scanning electron microscopy (SEM); their swelling behavior against saline solution was explored and their in vitro cytotoxicity was evaluated. Further, in order to elucidate kinetic aspects regarding the ternary system p(HEMA-co-dDMA-co-AA), a mathematical model of the reactivity ratios of the comonomers in the terpolymer has been conceived and analyzed. An intensified tendency of AA units accumulation in the copolymer has been noticed, in spite of HEMA units, while dDMA conserves in the copolymer the fraction from the feed. Three compositions have been selected for nafcillin-loading and their in vitro release capacity was evaluated. The compositions of 80:10:10 and 75:10:15 M ratios appear suitable for further in vivo testing, in order to be used as drug delivery systems in the treatment of different osseous diseases.

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1 Introduction

In the last few years, polymeric materials have been designed and proposed as matrices or depot systems for injectable or implantable systems or devices [1–7]. A particular approach towards an improved use of drugs for therapeutic applications is the design of polymeric pro-drugs or polymer–drug conjugates. Polymer chemists started to link drugs to polymers in order to improve their efficiency since the 1950s. At that time, they were mainly focusing on the chemistry itself, and different classes of polymers were covalently combined with a variety of drugs. The biological aspects for the design of polymeric prodrugs were hardly taken into consideration.

The first rational model for pharmacologically active polymers was proposed by Ringsdorf in 1975 [8], who recognized the immense potential of polymeric prodrugs. The model mainly consisted of five components: the polymeric backbone, the drug, the spacer, the targeting group, and the solubilizing agent. The polymeric carrier can be either an inert polymer or a biodegradable polymer. The drug can be fixed directly or via a spacer group onto the polymer backbone. The proper selection of this spacer brings the opportunity of controlling the site and the rate of release of the active drug from the conjugate by hydrolytic or enzymatic cleavage.

Treatment of osteomyelitis in most patients requires a lengthy regimen of parenteral antibiotic therapy and surgical removal of all necrotic, avascular, infected bone and soft tissue. Optimally, culture-directed antimicrobial therapy should be initiated after complete surgical debridement and after microbial confirmation of the diagnosis by biopsy [9, 10]. Generally, antibiotic therapy is maintained for at least 5 days. Inadequate debridement is a frequent

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Research Article

Direct Synthesis and Morphological Characterization of Gold-Dendrimer Nanocomposites Prepared Using PAMAM Succinamic Acid Dendrimers: Preliminary Study of the Calcification Potential

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Gold-dendrimer nanocomposites were obtained for the first time by a simple colloidal approach based on the use of polyamidoamine dendrimers with succinamic acid terminal groups and dodecanediamine core. Spherical and highly crystalline nanoparticles with dimensions between 3 nm and 60 nm, and size-polydispersity depending on the synthesis conditions, have been generated. The influence of the stoichiometric ratio and the structural and architectural features of the dendrimers on the properties of the nanocomposites has been described. The self-assembling behaviour of these materials produces gold-dendrimer nanostructured porous networks with variable density, porosity, and composition. The investigations of the reaction systems, by TEM, at two postsynthesis moments, allowed to preliminary establish the control over the properties of the nanocomposite products. Furthermore, this study allowed better understanding of the mechanism of nanocomposite generation. Impressively, in the early stages of the synthesis, the organization of gold inside the dendrimer molecules has been evidenced by micrographs. Growth and ripening mechanisms further lead to nanoparticles with typical characteristics. The potential of such nanocomposite particles to induce calcification when coating a polymer substrate was also investigated.

1. Introduction

As we are contemplating the extraordinary scientific and technological progress, "bio-" and "nano-" became nowadays common prefixes characterizing high-tech materials and devices. The interest and awareness of scientists of the use of gold and silver nanoparticles in various applications including biomedical uses have increased tremendously in the last ten years [1–11].

Obtaining noble metals nanoparticles in the presence of dendrimers represents nowadays a common procedure [1, 11–22]. However, the concept of silver- and gold-dendrimer nanocomposites is not new; it was developed approximately 17 years ago and it was based on the immobilization of preorganized metal ions in dendrimer hosts [12]. Dendrimers are well-known globular macromolecules presenting a typical tree-like architecture divergent from a central core and defined yet variable multifunctionality. They are interesting templates and reactive containers for noble metal precursors, able to initiate and direct the growth of the metallic nanometric crystals within a framework. Nevertheless, they act as stabilizers and/or encapsulating hosts. The main roles played by dendrimers, according to the original "dendrimer nanocomposite concept" introduced through the pioneering work done by Zawodzinki, Balogh, Tomalia, and Crooks, are as follows: (1) preorganization of ions involving guest-host interactions and (2) nanoreactor for *in situ* reduction reactions [12]. Furthermore, different morphological features such as shape, size, and size-distribution can be controlled through a rational combination of reagents and reaction conditions. Different parameters such as the dendrimer type

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Epoxy-mediated Immobilization of PAMAM Dendrimers Methacrylic Hydrogels
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EPOXY-MEDIATED IMMOBILIZATION OF PAMAM DENDRIMERS ON METHACRYLIC HYDROGELS

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This work reports the synthesis of a hybrid material containing NH_2-ending PAMAM. HEMA and epoxy propyl methacrylate were copolymerized to generate a polymer substrate. PAMAM was chemically bound on this matrix. ATR-FTIR and TNBS test confirmed the success of the reaction. ATR-FTIR showed that the dendritic component is responsible for apatite deposition after incubation in SBF, through calcium complexation both by NH_2 and amide C=O. Increasing the generation of the dendrimer leads to intensifying the biomineralization. This study supports the idea that amine-ending PAMAM induce biomineralization and demonstrates that these hybrids are promising materials suitable as osteoconductive bone grafts.

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Keywords: polymer hybrid, PAMAM, covalent immobilization, biomineralisation

1. Introduction

This study is aimed at the development of synthetic bone replacement biomaterials based on polymers inducing biomineralisation phenomena. Nowadays, the orthopaedic replacing surgery is using bone reconstruction fillers consisting in biomaterials with osteoinductive, osteoconductive or filling properties [1-4]. Hydroxyapatite (HA), the main mineral component of the natural bone, could be spontaneously produced after the implantation of a filler (cement or graft) using polymeric materials with special functionality. Compared to synthetic HA-polymer composites, the *in situ* HA-forming ones would provide a more suitable biological and durable solution for bone repair based on the patient's own tissue.

Extensive efforts were dedicated to the analysis of the induction of the mineralization of a synthetic or natural matrix, and the complexity of this phenomenon is impressive. However, it was concluded that there are numerous factors enhancing the mineralization occurrence in the presence of calcium and phosphate ions in the proximity of the implant. The most important influence was noticed for negatively and positively charged groups at physiological pH, that present an well known potential as heterogeneous nucleators of HA through calcium and phosphate ions capturing from the surrounding physiological fluids [2,3,5-12].

This study was based on the idea that a defined chemical functionality could lead to the nucleation and crystal growth of inorganic materials of HA-type. To provide this controlled distribution of charged groups, ***dendrimers*** have been selected as active component of the biomaterials in order to in situ create HA. These fascinating macromolecules have tree-like structures, with "branches" consisting in repeating units divergently emerging from a central core. For this work we have selected polyamidoamine (PAMAM) molecules; they are synthetic proteins, with globular shape in solution and presenting a wide range of external reactive groups. The presence of this external reactive shell is very useful for an important set of biomedical applications [13-15], based on the chemical binding of different substances of interest like drugs, enzymes, proteins, genes, dyes,.

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Lungu, A., ***Stancu, I.C.***, Rusen, E., Marculescu, B., Iovu, H.
Studies concerning the chemical immobilization of dendrimers on macroporous polymer matrix
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Studies concerning the chemical immobilization of dendrimers on macroporous polymer matrix

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A highly innovative combination of dendrimers with non-biodegradable host polymers (poly(2-hydroxyethyl methacrylate)) (PHEMA) was researched in order to obtain a completely new approach to bone regeneration. This study was aimed at the development of hybrid materials Polymer (PHEMA) - Polyamidoamine dendrimers (PAMAM), as smart biomaterials with Hydroxyapatite (HA) forming ability. Besides the capacity to form HA when implanted, these hybrids are designed with special macroporous interconnected architecture similar to that characteristic to the trabecular bone. The success of the binding of PAMAM on the surface of PHEMA matrix was checked through FTIR analyses. The hybrids will be further characterized and *in vitro* evaluated with respect to their capacity to initiate HA formation when used as bone grafts with osteoconductive properties.

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Keywords: Hybrid, Dendrimer, Polymer, Immobilization, Biomineralisation

1. Introduction

Current treatments of large bone defects mainly focus on the reconstruction of the defect using biomaterials with osteoinductive, osteoconductive or filling properties [1-4]. Polymeric materials which allow mineral formation are very important in orthopedics because their *in situ* transformation in composites polymer-HA similar to the bone natural ones. Compared to the synthetic composites, the *in situ* HA-forming ones offer a more suitable biological and durable solution for bone repair based on the patient's own tissue.

Mineralization of a synthetic or natural matrix is a complex phenomenon. There are numerous factors deciding the mineralization occurrence, but the presence of calcium and phosphate ions in the proximity of the implant represents the *sine qua non* condition. Calcium ions are provided by the surrounding cells and circulating fluids. Phosphate ions are supplied by the hydrolysis of phosphoesters or phosphoproteins, from circulating ions and/or from the breakdown of pyrophosphate [5]. Negatively and positively charged groups at physiological pH have well known potential as heterogeneous nucleation of HA through calcium and phosphate ions capturing from the surrounding fluids [2,3,6-13].

Starting from the idea that defined chemical functionality can decide on the nucleation and crystal growth of inorganic materials, ***dendrimers and hyper-branched polymers*** have been proposed and researched as ***templates for the formation of biominerals***, mainly leading to materials with well defined shapes and properties [14]. This study was aimed at the development of new hybrid materials combining a macroporous polymer matrix consisting in PHEMA with the mineralization potential of globular dendrimers with different functionality (see Fig. 1).

Dendrimers are nanometer-sized macromolecules, with tree-like or star-like structure, containing an important number of terminal groups that can be modified to suit a specific application. Several dendritic structures are commercially available; among them, PAMAM class represents by far the most extensively researched for biomedical applications [15-17]. They are available under a wide range of functional ending-groups appropriate to specific modifications.

All these considerations made us to choose PAMAM dendrimers as further templates for HA formation on the surface of the polymeric material. Different generations of PAMAM with $-NH_2$ and –COOH functional end-groups were used.

PHEMA was selected as hybrid matrix due to its biocompatibility and suitability for hard tissue replacement applications as well as for its bone filling well-known potential.

The work followed two main directions: 1) the synthesis of a macroporous PHEMA matrix with interconnected open porosity; 2) the chemical binding of globular dendrimers on the surface of PHEMA porous scaffolds.

This communication reports on the modification of the PHEMA surface with dendritic molecules. The evaluation of the success of the reaction was performed by infrared spectroscopy.

2. Experimental

Materials

The monomer 2-hydroxyethyl methacrylate (HEMA) was used after distillation under reduced atmosphere. Benzoyl peroxide (BPO) and N,N-dimethyl–p-toluidine (NNDMpT) were used to initiate the polymerization. Poly(methyl methacrylate) (PMMA) beads with average

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In this work, we focused on the potential of biogenous mineral from Cuttlefish bone for inducing biomimetic mineralization with further biomedical applications. We demonstrate the formation of strong and flexible hydrogels via physical immobilization of cuttlefish bone powder in the presence of bovine gelatin and alginate. The properties of hydrogels loaded with biogenous mineral, with a commercial bone substitute, with commercial nano-hydroxyapatite and in situ generated hydroxyapatite. In vitro cell adhesion tests demonstrated that the new developed hydrogels showed a promising cell adhesion.

Keywords: cuttlefish bone, mineral phase, gelatin-alginate hydrogels, biocompatibility

Healing of fractures with loss of tissue, various types of bone defects, osteomyelitis, non-union, and arthrodesis continue to be major challenges in orthopedic surgery [1]. Autologous bone allografts have several excellent organizational characteristics, but the presence of immune rejection, diseases, and high costs for sample preparation, handling, and storage, make their usage a very restricted one [2].

Thus, scientists are constantly searching for alternative bone fillers [3]. Natural bio-products are becoming increasingly important for the preparation of new materials [4]. In the last years, *cuttlefish bone* has drowned an increased interest [5-7]. Due to its aragonite pillar-like structure, its feasibility as bone graft has been investigated *in vitro* [7]. It can be obtained easily and inexpensively from all the seas of the world, it is cheap [6], it can be shaped easily due to its morphology and mineral composition, it is compatible with other types of bone structure and it has high osteoinductive capacity [8].

The mechanism governing the superior performances of hard tissue in contact with calcium based minerals ensue from the fact that bone cells are naturally accustomed with hydroxyapatite physiological environment, represented by the natural constituents of healthy bone and teeth [9-12]. Pursuant to the requirement of low cost and easy preparation with good performances (as mechanical and biological ones), cuttlefish bone represent a great alternative as mineral phase filler for polymeric materials [13]. One type of polymers that has been extensively applied for bone tissue regeneration includes hydrogels such as collagen, gelatin, alginates, chitosan and glycosaminoglycans [14-16]. Most hydrogels lack mechanical and/or thermal stability at physiological conditions, therefore cross-linking procedures and reinforcement with mineral phase have become practically inevitable due to their capacity to combine the tailorable properties of the bioactivity of the biopolymers with the properties of a calcium based mineral [16 – 18].

In this study, hydrogels based on gelatin and alginate, loaded with cuttlefish bone powder have been synthesized and characterized. To prove the great potential of this biogenous mineral for bone applications, another series of hydrogels was prepared. In this case well known mineral phase was loaded into the hydrogels such as: commercially available bone substitute, nano-hydroxyapatite and *in situ* generated nano-hydroxyapatite. The properties of all the materials were compared. The results lead to the conclusion that cuttlefish bone is indeed a promising bone filler due to the increased mechanical properties of the hybrid hydrogel, good biocompatibility, and tunable water affinity.

Experimental part

Materials and methods

Sodium alginate (alginic acid sodium salt from marine brown algae) with medium viscosity, gelatin from bovine skin (Type B, suitable for cell culture), glutaraldehyde (GA), calcium chloride ($CaCl_2$), sodium phosphate (Na_2HPO_4) and nano-hydroxyapatite (n-Hap) were purchased from Sigma Aldrich. Glutaraldehyde and $CaCl_2$ were used as cross-linkers. *Cuttlefish bone* (CB) was purchased from pet shops in Romania where it is sold as calcium supplement for birds. Eurocer 400 is a biphasic (hydroxyapatite 55% and tricalcium phosphate 45%) commercial synthetic bone substitute (BS) developed by FH Orthopedics. $CaCl_2$ and Na_2HPO_4 were used as mineralization precursors.

Powder preparation

The CB was cut in small cubes and extensively washed with double distilled water for 3 days at room temperature (RT). In a further step the CB cubes were dried and subsequently finely milled to a powder. The separation of the fine powder was performed through several decanting steps from water.

The same procedure of obtaining fine powder was applied for the commercial BS.

Synthesis of the hybrid hydrogels

The hybrid hydrogels were obtained through a three-step procedure: (1) dispersion of the mineral phase into the aqueous polymer solution, (2) physical gelation at 4°C and (3) cross-linking of the final compositions

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EMERGING GROUP LEADERS: RESEARCH AND REFLECTIONS ON CAREER GOALS

Original Research

Nanocomposite particles with improved microstructure for 3D culture systems and bone regeneration

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Abstract Nano-apatite and gelatin-alginate hydrogel microparticles have been prepared by a one-step synthesis combined with electrostatic bead generation, for the reconstruction of bone defects. Based on the analysis of bone composition, architecture and embryonic intramembranous ossification, a bio-inspired fabrication has been developed. Accordingly, the mineral phase has been in situ synthesized, calcifying the hydrogel matrix while the latter was crosslinked, finally generating microparticles that can assemble into a bone defect to ensure interconnected pores. Although nano-apatite—biopolymer composites have been widely investigated, microstructural optimization to provide improved distribution and stability of the mineral is rarely achieved. The optimization of the developed method progressively resulted in two types of formulations (15P and 7.5P), with 15 and 7.5 (wt%) phosphate content in the initial precursor. The osteolytic potential was investigated using differentiated macrophages. A commercially available calcium phosphate bone graft substitute (Eurocer 400) was incorporated into the hydrogel, and the obtained composites were in vitro tested for comparison. The cytocompatibility of the microparticles was studied with mouse osteoblast-like cell line MC3T3-E1. Results indicated the best in vitro performance have been obtained for the sample loaded with 7.5P. Preliminary evaluation of biocompatibility into a critical size (3 mm) defect in rabbits showed that 7.5P nanocomposite is associated with newly formed bone in the proximity of the microparticles, after 28 days.

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Bicomponent Hydrogels Based on Methacryloyl Derivatives of Gelatin and Mucin with Potential Wound Dressing Applications

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The present paper reports the first attempt to synthesize bicomponent hydrogels based on methacryloyl derivatives of gelatin (GelMA) and mucin (MuMA) with different compositions, with potential as wound dressings. While gelatin is widely investigated and used to fabricate scaffolds and coatings stimulating cell interactions and tissue regeneration, mucin - a macromolecule which covers the wet epithelia - remains yet under exploited as biomaterial. The influence of MuMA content on various parameters such as the affinity for aqueous media, stability in simulated physiologic media and the rheologic behavior was investigated. Also, the preliminary assessment of the drug release potential and biocompatibility were performed. The materials' water uptake capacity and rheologic behavior depend on the pH value of the incubation media, while their composition influences the drug release capacity and cells-scaffold interactions.

Keywords: Methacryloyl gelatin, methacryloyl mucin, network-forming polymerization, hydrogels

Skin represents the largest organ of the body and its primary role is to act as a shield between the body and the external factors. When skin is ruptured, covering the wound is necessary in order to protect the body from possible microbial attack and fluid loss [1]. Minor dermal lesions such as scratches might heal without scars, but large full-thickness defects require surgical intervention and may lead to tissue contraction and formation of unaesthetic marks.

In the early 80s' a significant breakthrough was made in the field of dermal treatments designed for large wounds, by the development of a skin substitute based on collagen and glycosaminoglycans, subsequently commercialized under the name of Integra Artificial Skin®. Despite further advances in the fields of medicine and technology, and the increased availability of new relevant products, an ideal skin product for skin replacement and repair has not been yet found and autografts still represent the *golden standard* [1]. According to a survey performed by Selig et al. among clinicians, an ideal wound dressing should be non-adhesive to the wound bed and easy to remove, absorbent, available in a large range of sizes and should possess antimicrobial properties [2]. In addition, these materials should positively influence the regeneration of the affected tissue.

Considering the previously described features, hydrogels show great potential for such applications, especially due to their functional resemblance to the natural extracellular matrix (ECM) and their ability to absorb and retain large amounts of water without dissolving [3]. Moreover, hydrogels can easily be loaded with various drugs, such as local anesthetics, antibiotics or pain-relievers [4].

Gelatin represents a main actor in the development of hydrogels with applications in the field of soft tissue engineering due its biocompatibility, biodegradability, non-toxicity, non-immunology and low price. The use of gelatin as wound dressing has been limited due to its solubility in aqueous media, poor thermal and mechanical behavior. Gelatin's methacryloyl derivative has been obtained through the direct reaction with the methacrylic anhydride, as first reported by Van Den Bulcke et al. [5], and it is currently used to obtain simulated physiological microenvironments [6–10]. Methacryloyl gelatin (GelMA) can be further polymerized similarly to a synthetic monomer, leading to biocompatible, mechanically and thermally stable, insoluble materials with tunable properties (e.g: porosity, degradability, water uptake capacity) [3].

Mucin is a high-molecular mass glycoprotein which covers the wet epithelia, its main function being to protect the organism from small particles, viruses or bacteria [11]. Its unique structure consists of a protein backbone amounting for about 20% of its total mass, on which highly glycosylated carbohydrates are radially attached [11,12]. This molecule seems appealing for modulating gelatin's properties. There are only a few studies regarding the use of mucin, mostly for drug-delivery applications [11,13], as biological surfactants [14–16] or anti-bacterial barrier [12,17–19]. To the best of our knowledge, methacryloyl mucin (MuMA) has been investigated only for sustained drug delivery applications [11], while a system formed by the GelMA and MuMA has never been synthesized before.

This paper presents the first attempt regarding the synthesis and characterization of such bicomponent systems. The aqueous media uptake capacity, stability and

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