CHEM MASTERY

DEPARTMENT OF PHARMACEUTICAL CHEMISTRY - NEWS LETTER

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ISSUE HIGHLIGHTS

CARBON NANOTUBE REINFORCEMENT OF DNA-SILICA NANOCOMPOSITES AS CELL INSTRUCTIVE BIOCOATINGS

Biomedical applications require substrata that allow for the grafting, colonization and control of eukaryotic cells. Currently available materials are often limited by insufficient possibilities for the integration of biological functions and means for tuning the mechanical properties. We report on tailorable nanocomposite materials in which silica nanoparticles are interwoven with carbon nanotubes by DNA polymerization. The modular, well controllable and scalable synthesis yields materials whose composition can be gradually adjusted to produce synergistic, non-linear mechanical stiffness and viscosity properties. The materials were exploited as substrata that outperform conventional culture surfaces in the ability to control cellular adhesion, proliferation and transmigration through the hydrogel matrix. The composite materials also enable the construction of layered cell architectures, the expansion of embryonic stem cells by simplified cultivation methods and the on-demand release of uniformly sized stem cell spheroids

The design of novel, programmable "intelligent" cell culture substrates to control the interaction of eukaryotic cells with technical surfaces is of paramount interest for biomedical applications, such as stem cell therapies or tissue engineering. These applications call for biocompatible materials with tunable physical properties in terms of porosity and elasticity, which can be functionalized with biomolecules, such as proteins, peptides, morphogens, and growth factors, and which can be degraded under mild conditions to release the cells or cell aggregates after cultivation. Synthetic hydrogels are very promising in this respect because their three-dimensional (3D) porous structure yields biocompatibility, high-water content, and tissue-like elastic properties that allow for effective permeation of oxygen and nutrients, which is crucial for cellular colonization.

While approaches have been developed for the systematic adjustment of the mechanical properties of organic hydrogels by cross-linking with nanoparticles, synthetic hydrogels may suffer from potential drawbacks due to adverse effects of chemical ingredients. Hydrogel materials from DNA offer advantages in this respect, as they can be produced using exclusively non-toxic biochemical reactions. These biopolymers can also be programmed very efficiently via their nucleic acid sequence in order to install shape memory persistence, molecular recognition capabilities and stimuli responsiveness, for example, to facilitate their degradation with a mild enzymatic treatment. However, the mechanical properties of DNA hydrogels are difficult to modify. A multitude of DNA-functionalized nanoparticles have been produced e.g. from gold, metalloxides, silica, or carbon nanotubes (CNT). DNA-decorated silica NPs (SiNP) have unique properties in terms of biocompatibility and synthetic accessibility. Since

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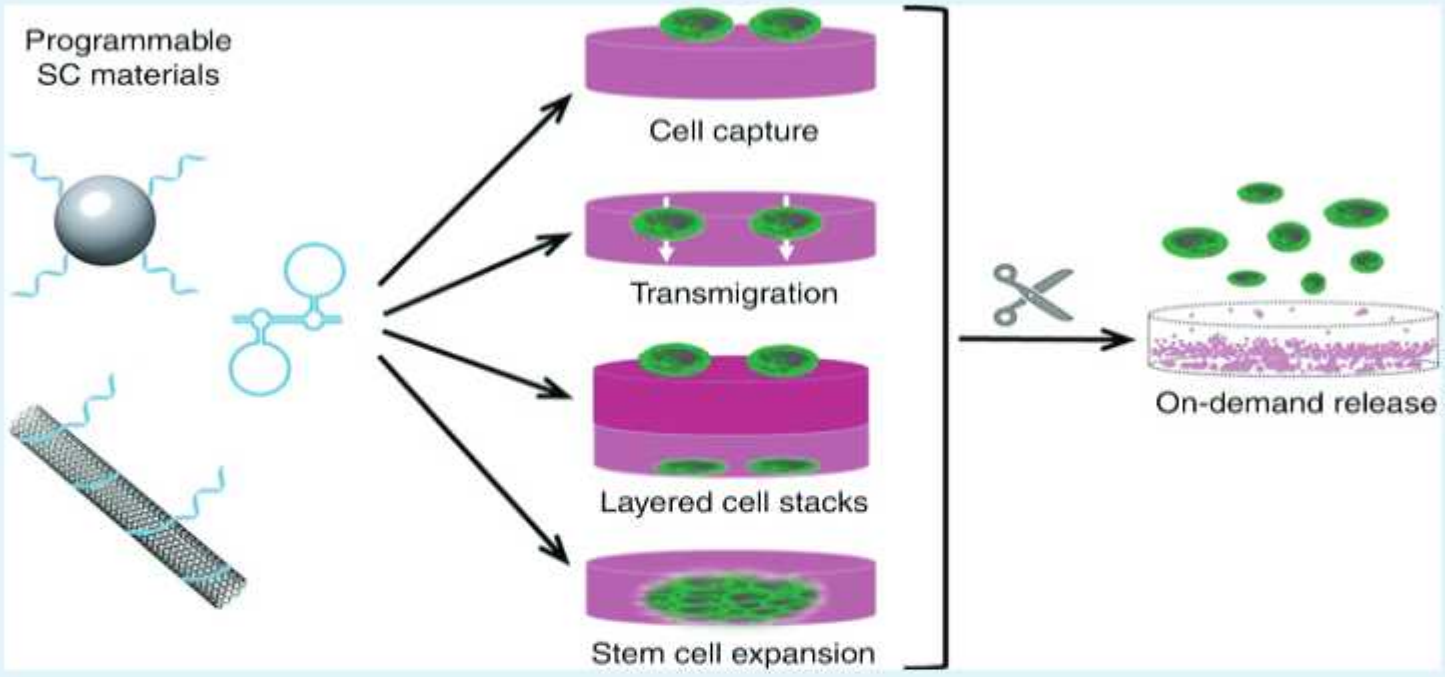
preliminary studies indicated the utility of CNT in reinforcing nanofiber networks and suggested good compatibility with DNA materials, we hypothesized that the combination of SiNP, CNT and DNA hydrogels should be able to produce mechanically adjustable materials that can be used to control cellular functions.

Here describe composites in which silica nanoparticles are interwoven with carbon nanotubes by DNA polymerization. The modular, well controllable and scalable synthesis yields materials whose composition can be gradually adjusted to produce synergistic, non-linear mechanical stiffness, and viscosity properties. The materials' tailorable elastic properties are used to control cellular adhesion, proliferation and transmigration through the hydrogel matrix. We also demonstrate controlled cell release under mild conditions. This allows for the construction of layered cell architectures, the expansion of embryonic stem cells by simplified cultivation methods and the production of uniformly sized stem cell spheroids (Fig. 1).



Since materials libraries can be readily constructed via automated synthesis, we believe that the materials have a high potential for fundamental studies and device applications in biomedical sciences

In conclusion, the developed class of nanocomposite DNA materials can be customized for cell culture applications by means of a series of set screws. Since the materials are readily obtained from DNA-modified nanoparticles through enzymatic biosynthesis, our synthetic approach is generic and applicable to a wide range of nanomaterials, whose composition can be gradually tuned at will. As demonstrated by variation of the SiNP:CNT mass ratio, this can lead to non-linear effects on the materials' physicochemical properties, such as mechanical stiffness and viscosity, which are fundamental for the establishment, maintenance and control of cellular systems. Our exemplary demonstration that cellular adhesion, propagation and motility can be controlled by adjustment of SiNP:CNT particle composition suggests that incorporation of particles from other materials and/or different size, aspect ratio, or binding valency will lead to an almost unlimited variety of designer materials. Importantly, this synthetic approach is amenable to automated synthesis as a means to create and screen libraries of materials for unpredictable properties that can arise from distinctive compositions of building blocks. As initial demonstration, it took advantage of this combinatorial approach by establishing substrata for control of cellular adhesion and transmigration through the hydrogel matrix. The composite materials could also be applied to enhance stem cell proliferation with concomitant preservation of their stemness to enable less complex cultivation procedures. Based on these measures, the composites clearly outperform conventional tissue culture substrata.Another important implication of this work arises from the fact that the materials display not only the features emerging from those of the crosslinked nanoparticles, such as cell attractiveness of SiNP and stiffness of CNT particles harnessed here. However, distinct bioinstructive

properties can be conveniently implemented into the materials through rational engineering of the connecting DNA polymer backbone. Here demonstrated incorporation of enzymatic restriction sites enabled the control of vertical transmigration, as well as the on-demand release of captured cells. These initial examples of "functionality by design" suggest that implementation of basic concepts of DNA nanotechnology can open the door to even more sophisticated materials that enable control of cell response.

Prepared by
Ayisha Nitha P.,
I Sem M.Pharm

DNA SEQUENCING USING GRAPHENE NANOPORES

DNA sequencing is the process of determining the exact order of the bases [A, T, G and C] in a molecule of DNA.

- Scientists will be able to detect the defective genes responsible for genetic diseases like Alzheimer's disease, cancer, diabetes etc and can replaced with the healthy ones.
- It is a promise for future to give patients precise personalized treatment developed on the basis of that patient's specific DNA sequence.
- In crime forensics- to identify a body & solving a crime: height, skeletal and facial features, skin colour etc of a person can be determined.
- Determine the paternity
- In agriculture- to make pest resistant plants, to increase productivity and quality of milk & meat etc.

DNA sequencing has come a long way since 1970s, when the first technique was introduced by Frederick Sanger. The technique involves 4 steps

- DNA amplification
- Sequencing reaction
- Separation and detection of the fragments
- Assembling of the sequenced parts of a gene

GRAPHENE NANOPORES

Graphene is a one atom thick sheet of C-atoms, arranged in a honey comb [hexagonal] lattice. Thickness is 0.3nm. It is thinnest & strongest known material and is very flexible. It is continuous and exhibit high crystal quality. It was considered as a 'material that could not exist' since it was isolated for the first time in 2004.

It is a great electrical conductor: Each atom is covalently bonded to three others; but since carbon has four valence electrons, one is left free - allowing graphene to conduct electricity. Electrons are able to flow as fast as 1/100th of the speed of light in vacuum. Graphene is transparent, cheap and plentiful. It is harder than diamond & 300 times harder than steel and stretchable up to 20% of its initial length. Single layer of graphene is only 0.3nm thick, smaller than the distance between 2 bases. When a DNA strand passes through it, a single nucleotide can block the pore at any moment. These makes graphene nanopore a promising device for DNA sequencing.

The pores are obtained by placing a graphene sheet over a 5µm sized hole in a SiN membrane and drilling a nanosized [about 5nm] hole in the graphene using highly focused electron beam of a Transmission Electron Microscope [TEM]. Added a layer of Titanium oxide to the graphene membrane to make the hydrophobic graphene more wettable. The layer is mounted into a microfluidic flow cell, added a 1M saline solution [1M KCl, pH-8.0] on both sides of the membrane. A voltage is applied across the membrane for which the current from ion transport through pore is measured. Single or double stranded DNA was driven electrophoretically through the nanopore as a long string. Each nucleotide may obstruct the nanopore to a different characteristic degree and the amount of the current passing through the pore varies depending on the type of nucleotide. Each temporary drop in measured conductance arises from a single nucleotide that translocate through the pore.

Advantages

- Excellent conductivity.
- Chemically inert & stable in operational environment.
- Low thickness.
- Cheap.
- Fast sequencing- 10 genome/day.
- Direct sequencing without the need of an intervening PCR amplification or a chemical labeling step or the need for optical instrumentation [lasers] to identify the chemical label.

Conclusion

- This low-cost, ultra-fast & accurate DNA sequencing could revolutionize both healthcare and biomedical research, and lead to major advances in drug development, preventative medicine and personalized medicine.
- Several challenges still remain to be overcome including controlling the speed with which DNA threads through the pore.
- DNA sequencing could get a lot faster and cheaper and thus closer to routine use in clinical diagnostics.

Prepared by
Mrs. Ayswarya K,
Assistant Professor

DEPARTMENT ACTIVITIES

ON GOING RESEARCH PROJECTS:

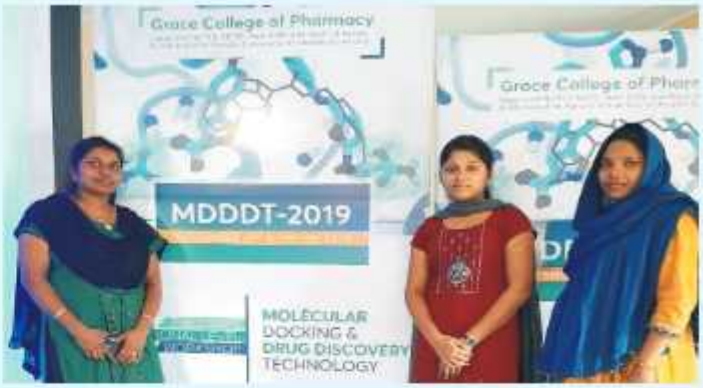
Following are the research projects from Department of Pharmaceutical Chemistry and Pharmaceutical Analysis for Post Graduate students in the academic year 2019-2020:

Students Name	Project Title	Guided by
Amita S.Menon	Isolation, evaluation and analytical validation of newly formulated arishta from *Ficus religiosa* root bark	Dr. Biju C. R.
Sruthi R.	Formulation, standardization and analytical validation of newly formulated ointment containing *Calendula officinalis* and *Echinacea purpurae* mother tinctures	Dr. Biju C. R.
Anjali V.P	Design, synthesis and invitro antidiabetic potential of piperidinyl coumarin derivatives	Dr. Shiny George
Shahana C	Insilico docking studies, synthesis and biological evaluation of pyrrole linked thiazolidinedione derivatives	Mr. Arunlal V. B

SEMINARS/ CONFERENCES ATTENDED:

Dr. G. Babu, Mrs. Binjusha and **Ms. Teena Thomas** along with 5th semester B.Pharm and 1st semseter M.Pharm students has participated in AICTE sponsored International Conference on recent trends in nano biogovernance on 27.09.2019 and 28.09.2019 at Al Shifa College of Pharmacy, Perinthalmanna, Kerala. Dr. G. Babu chaired one session too.

Mrs. Shalima N. K. and **II year M. Pharm Pharmaceutical Chemistry students** participated in two days National level Workshop on Molecular Docking and Drug Discovery Technology (MDDDT-2019) organized by Department of Pharmaceutical Chemistry at Grace College of Pharmacy, Palakkad, Kerala on 27.09.2019 and 28.09.2019.



Dr. Shiny George and **I year M. Pharm Pharmaceutical Chemistry students** attended National Conference on Molecular tools and disease diagnosis organized by Department of Biotechnology Engineering, Sahrdaya College of Engineering & Technology, Kodakara, Kerala on 03.10.2019 - 05.10.2019.

Dr. Biju C. R. has invited as a speaker in Continuing Education Program conducted by Kerala State Pharmacy Council, Thiruvananthapuram. He has given a seminar on the topic "Good Pharmacy Practice" at Edappal hospital, Edappal, Malappuram on 06.10.2019.

Mrs. Nimmi M., Dr. M. Kumanan and **Mrs. Bhavya Sivadas** accompanied 5th semester B. Pharm students for one day visit to Vaidyaratnam P.S Varier's Arya Vaidya Sala manufacturing unit at Kottakkal on 21.10.2019.

Ms. Neethu Dasan, Dr. Siraj Sundaran and **Mrs. Binjusha** along with **IV[th] Pharm D. students** participated as delegate and attended the scientific sessions of 2nd Pharmaceutical Sciences Congress-2019 organised at St.Petees Institute of Pharmaceutical Sciences, Warangal, Telangana, India on 1.11.2019 and 2.11.2019.

Dr. Shiny George, Mr. Arunlal V.B, Mrs. Anjali Narayanan, I and **II year M. Pharm Pharmaceutical Chemistry students** along with 6 B. Pharm students attended National Seminar on New Insights in Pharmacogenomics and Recent Advances in Computer Aided Drug Design held at JDT Islam College of Pharmacy, Calicut on 16.11.2019. Dr. Shiny George chaired one session and evaluated poster presentation also.

PAPER PUBLICATIONS

Biju C. R. *et al,*

Activities of *Salix purpurea* (Purple willow bark)- A review, Journal of Pharmacy and Pharmaceutical Research, 16(1), 2019, 372-382.

PAPER PRESENTATION

Dr. Shiny George presented paper on "Insilico studies and synthesis of novel mycobacterium tuberculosis enoyl-acp reductase and CYP-51 inhibitors" during National Conference on Molecular tools and Disease diagnosis organized by Department of Biotechnology Engineering, Sahrdaya College of Engineering & Technology, Kodakara, Kerala on 03.10.2019 - 05.10.2019.

ACHIEVEMENTS

Mrs. Ayswarya K has completed certificate programme in Health Science Education Technology (C-HSET) conducted at KUHS Academic Staff College in 2019 batch on 23.10.2019.

Dr. G. Babu has honored with "Dr. APJ ABDUL KALAM AWARD FOR TEACHING EXCELLENCE-2019 of Marina Labs Research and Development, Chennai on 24.11.2019.

SOCIAL ACTIVITY

Mrs. Nimmy M., Mr. Arunlal V.B., Dr. Shiny George and **Mr. Mridul Mohan** accompanied Ist & IInd D.Pharm Students to Gender Park, Vellimadukunnu, Kozhikode on 12.07.2019 as part of NSS activity for cleaning of child welfare campus and oldage home premises. Also done health checkup for inmates of oldage home.

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