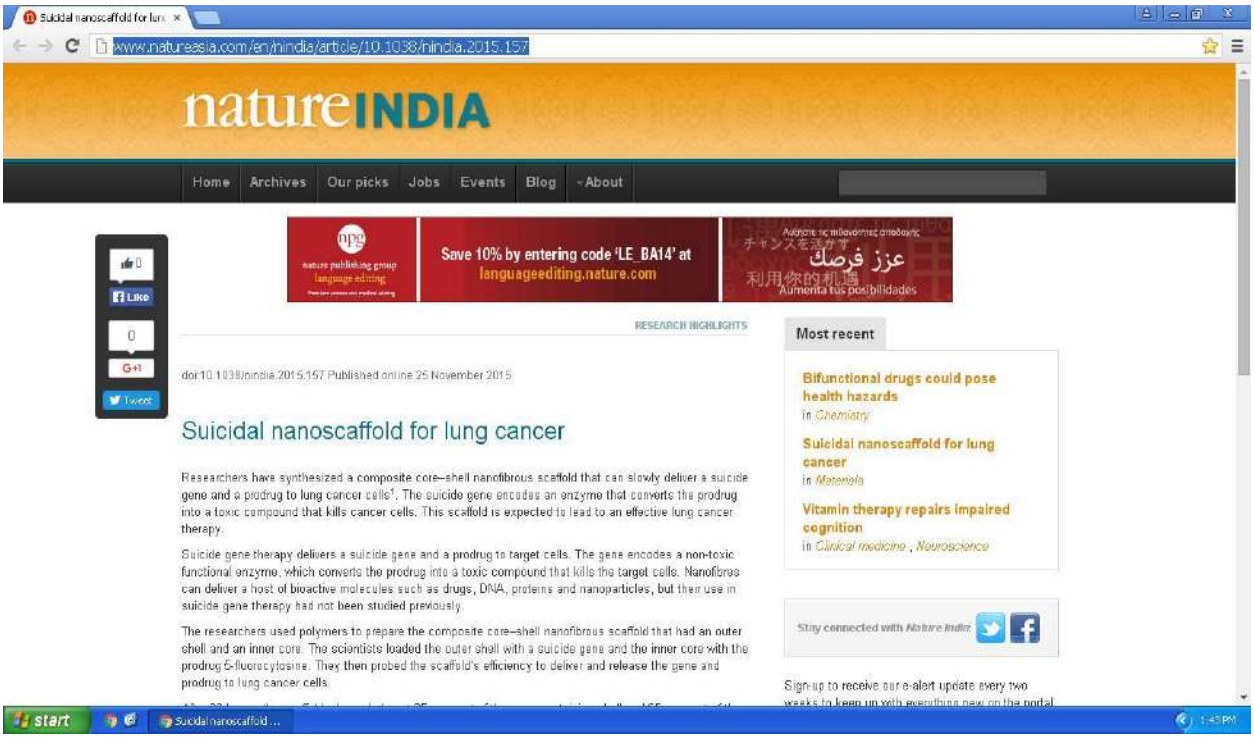
Currently his research group in nanobiotechnology laboratory at IIT Roorkee is working on the development of various polymer based nanocarriers for the delivery of several therapeutic agents and also exploring the possibilities of different biocompatible imaging agents for cancer diagnosis.

Nanofiber scaffold's ability to foster seemingly nonexistent interface with the cells enables them to effectively deliver various bioactive molecules to cells in the vicinity. Among such bioactive molecules, therapeutically active nucleic acid has been the most common candidate. In spite of such magnanimous efforts in this field, it remains a paradox that suicide gene delivery by nanofibers has never been sought for anticancer application. To investigate such a possibility, in the present work, a composite core–shell nanofiberous scaffold has been realized which could efficiently transfect suicide gene into cancer cells and simultaneously deliver prodrug, 5-Fluorocytosine (5-FC) in a controlled and sustained manner. The scaffold's ability to instigate apoptosis by suicide gene therapy in nonsmall lung cancer cells (A549) was ascertained at both phenotypic and genotypic levels. A cascade of events starting from suicide gene polyplex release from nanofibers, transfection, and expression of cytosine deaminase-uracil phosphoribosyltransferase (CD::UPRT) suicide gene by A549; subsequent prodrug release; and its metabolic conversion into toxic intermediates which finally culminates in host cells apoptosis has been monitored in a time-dependent manner. This work opens up new application avenues for nanofiber-based scaffolds which can effectively manage cancer prognosis.



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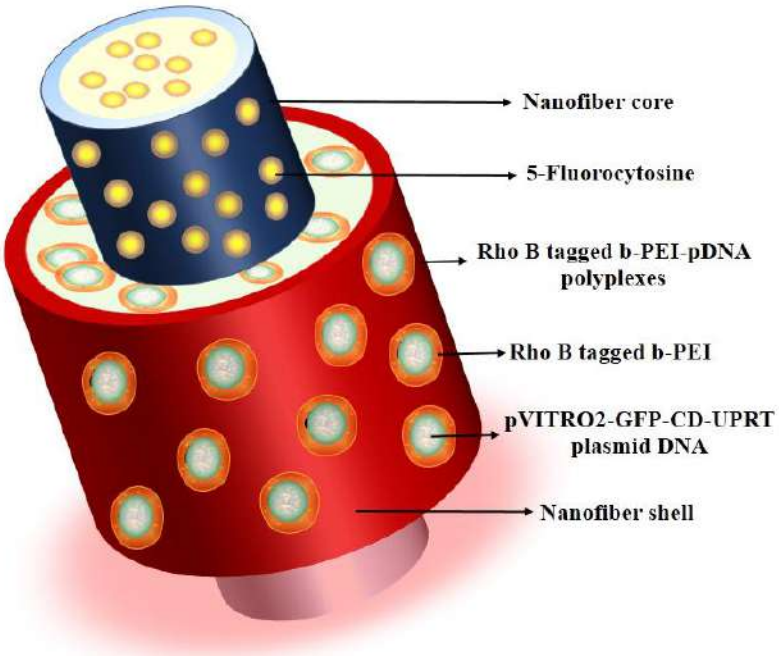
Bioactive Core–Shell Nanofiber Hybrid Scaffold for Efficient Suicide Gene Transfection and Subsequent Time Resolved Delivery of Prodrug for Anticancer Therapy

Uday Kumar Sukumar[†] and Gopinath Packirisamy[*,†,‡]

[†]Nanobiotechnology Laboratory, Centre for Nanotechnology, [‡]Department of Biotechnology, Indian Institute of Technology Roorkee, Roorkee, Uttarakhand-247667, India



Advanced nanomaterials integrating imaging and therapeutic modalities on a single platform offers a new horizon in current cancer treatment strategies. Recently, carbon dots (CQDs) have been successfully employed for bioimaging of cancer cells. In the present study, luminescent CQDs with anionic terminus and cationic acetylated G5 poly(amido amine) (G5-Ac85) dendrimers were combined via noncovalent interactions to form self-assembled fluorescent hybrids. The fluorescence of CQDs in hybrids is enhanced in the vicinity of primary amine groups of dendrimers, making them suitable as cellular imaging probes. Encapsulation of chemo-drug epirubicin (EPI) in the dendrimer interiors endowed the fluorescent hybrids with therapeutic potential. The *in vitro* release of an entrapped EPI drug from CQDs@EPI⊂G5-Ac85 hybrids was faster in an acidic environment than under physiological conditions. Herein, multifunctional CQDs@EPI⊂G5-Ac85 hybrids serve as a dual-emission delivery system, to track the intracellular distribution and cytotoxic effects of EPI drugs. Green emission properties of CQDs were used for fluorescence microscopic imaging and cellular uptake by flow cytometry. Cell cycle analysis, field-emission scanning electron microscopy (FE-SEM), reactive oxygen species

(ROS) generation, and up-regulation of apoptotic signaling genes unanimously demonstrated the apoptosis inducing ability of CQDs@EPI⊂G5-Ac85 hybrids in breast cancer (MCF-7) cells. Therefore, we have evaluated CQDs@EPI⊂G5-Ac85 hybrids as prospective candidates to achieve simultaneous imaging and drug delivery in cancer cells.

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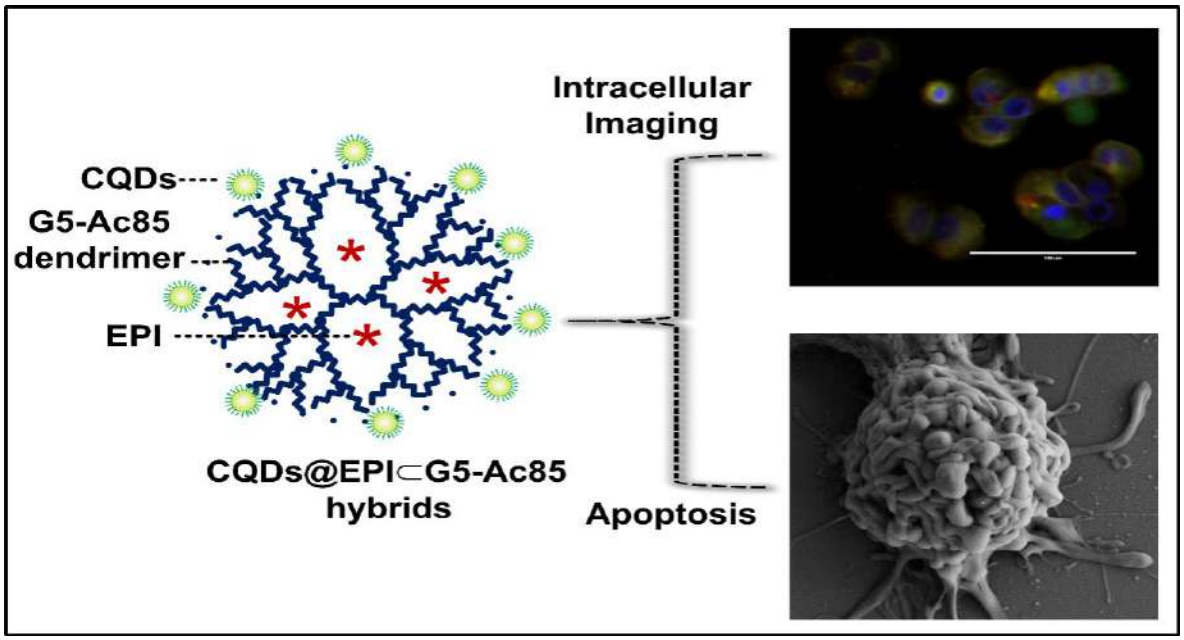
Self-Assembled Hybrids of Fluorescent Carbon Dots and PAMAM Dendrimers for Epirubicin Delivery and Intracellular Imaging

Ishita Matai,[†] Abhay Sachdev,[†] and P. Gopinath*[,†,‡]



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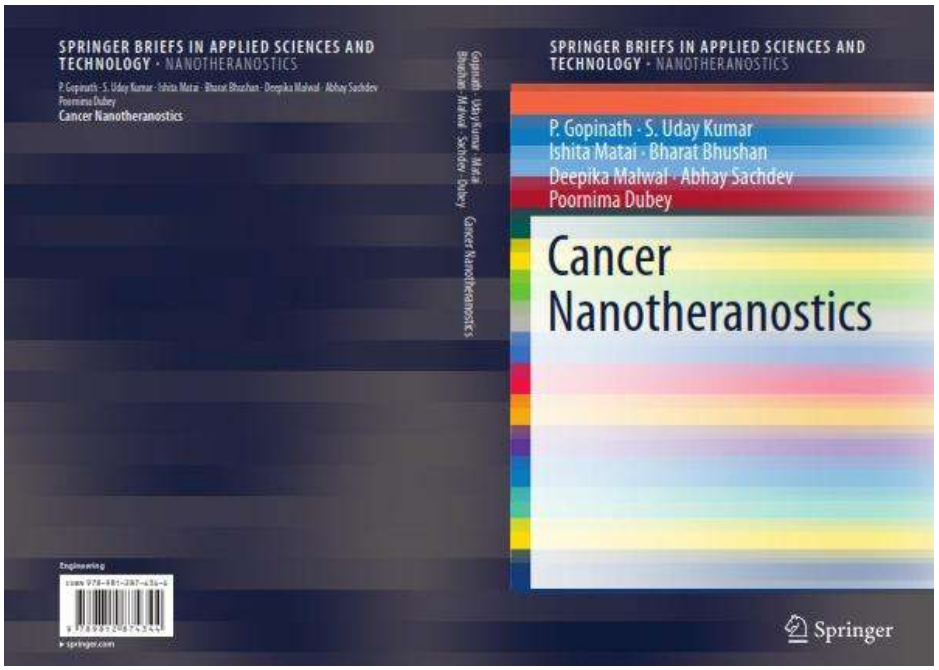
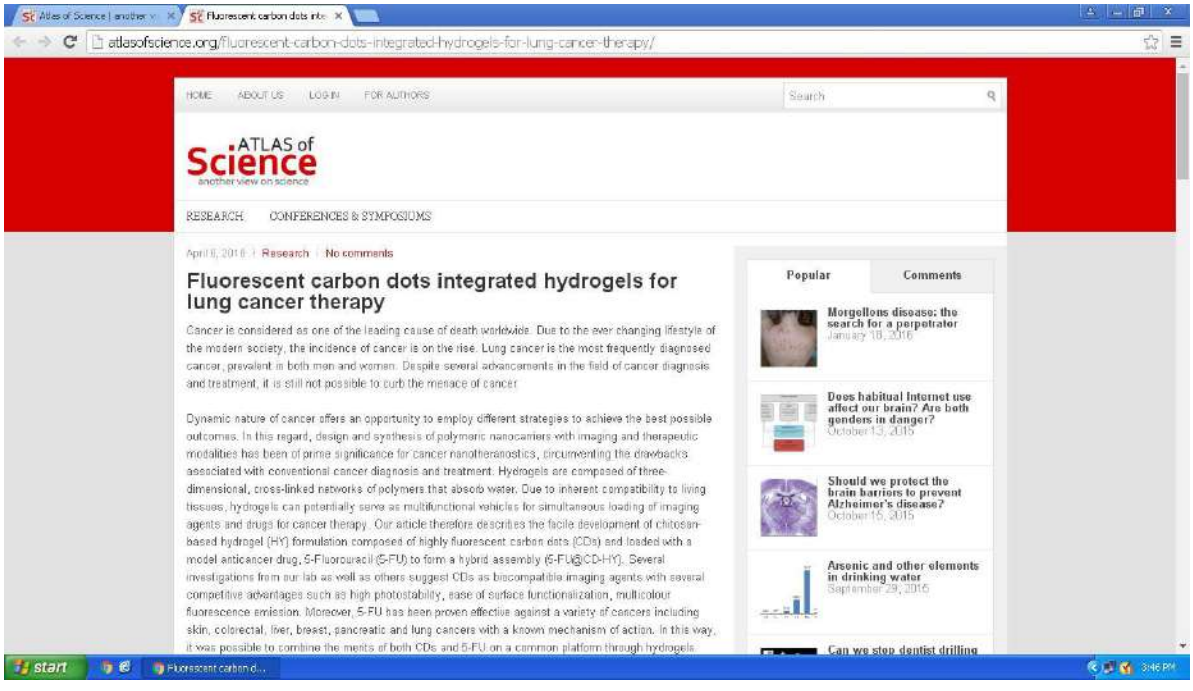
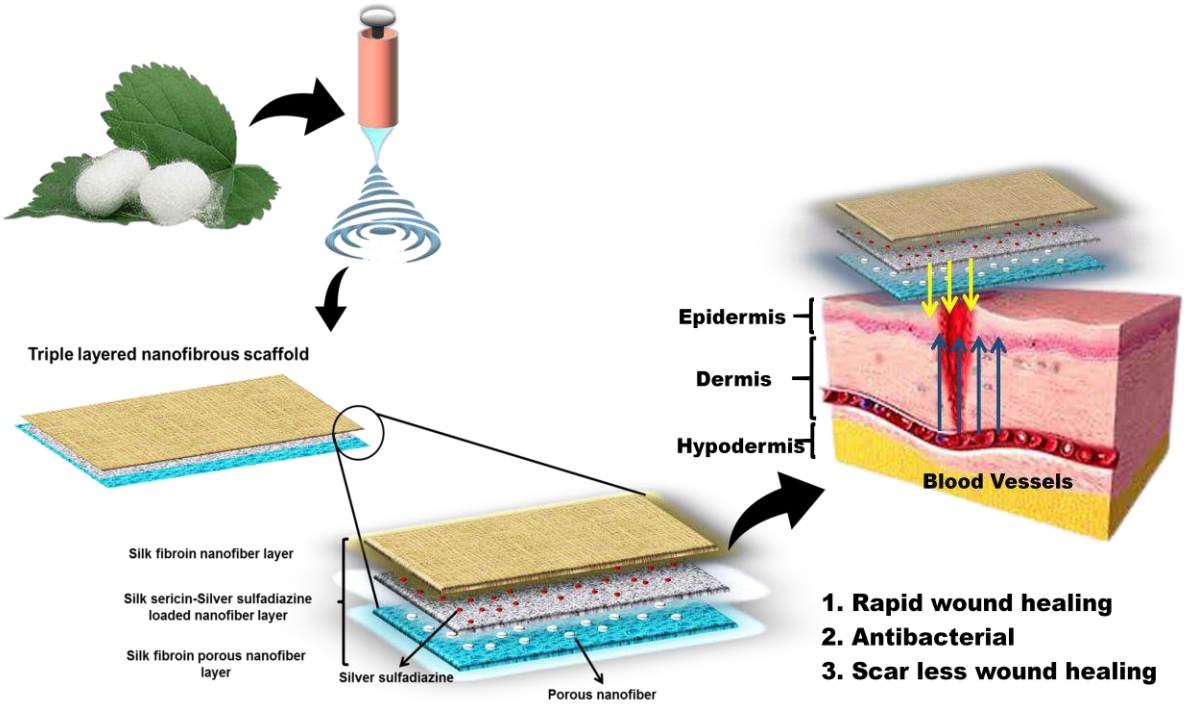
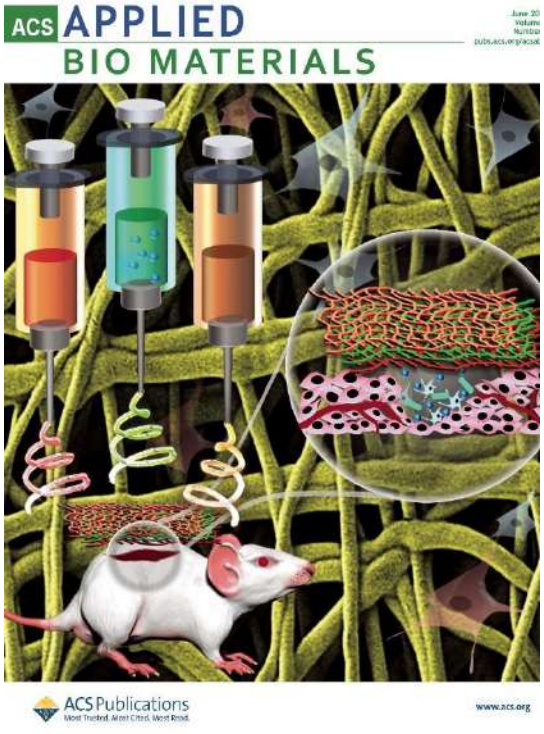


Multifunctional hydrogels offer a seemingly efficient system for delivery of drugs and bioimaging modalities. The present study deals with the facile development of chitosan-based hydrogel formulation composed of highly fluorescent carbon dots (CDs) and loaded with a model anticancer drug, 5-Fluorouracil (5-FU). Herein, CDs were embedded firmly within the hydrogel matrices (CD-HY) via non-covalent interactions during the ionic cross-linking reaction. Furthermore, these hydrogels could effectively encapsulate 5-FU through hydrophobic interactions to form 5-FU@CD-HY. In this way, it was possible to combine the merits of both CDs and 5-FU on a common platform for monitoring the cellular uptake as well as therapeutic effects. Field emission scanning electron microscopy (FE-SEM), transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA) illustrated the porous nature and formation of 5-FU@CD-HY. Besides, functional characteristics of 5-FU@CD-HY such as surface area, mechanical strength, swelling behavior and drug release were investigated. In vitro studies revealed the multifunctional aspects of 5-FU@CD-HY in monitoring the cellular uptake and inflicting apoptosis in A549 cells. Green fluorescence of CDs in 5-FU@CD-HY aided the qualitative and quantitative assessment of cellular uptake. In addition to this, the fluorescence of CDs could be used to detect apoptosis instigated by 5-FU, eliminating the need for multiplex dyes. Induction of apoptosis in 5-FU@CD-HY treated cells was evidenced by changes in cell cycle distributions and visualization of characteristic apoptotic bodies through FE-SEM. Apoptotic gene expression studies further elucidate the molecular mechanism involved in eliciting apoptosis. Thus, hydrogels mediated integration of fluorescent CDs with chemotherapeutic agents provides a new dimension for the potential use of hydrogels in cancer theranostics.



Recently, his team has also developed self-degrading biobandages for chronic diabetic wound healing which will revolutionize the wound dressing materials. This biobandages will overcome the drawbacks such as the lack of oxygen supply, non-degradable issues and are pain full adhesives. This self-degradable nanofibrous sandwich bandages have potential applications to accelerate the healing of diabetic wounds.





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Carica papaya loaded poly (vinyl alcohol)-gelatin nanofibrous scaffold for potential application in wound dressing

Jyoti Ahlawat[a,1], Vinay Kumar[a,1], P. Gopinath[a,b,*]

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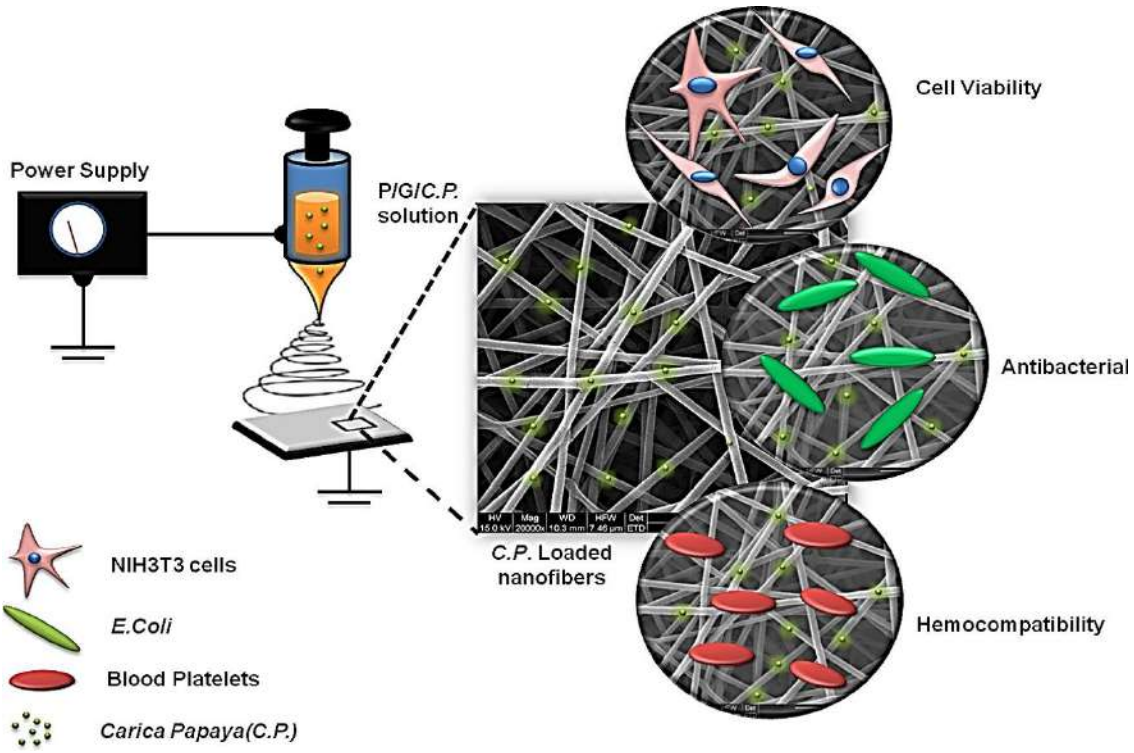
[b] Center for Nanotechnology, Indian Institute of Technology Roorkee, Roorkee 247667, Uttarakhand, India



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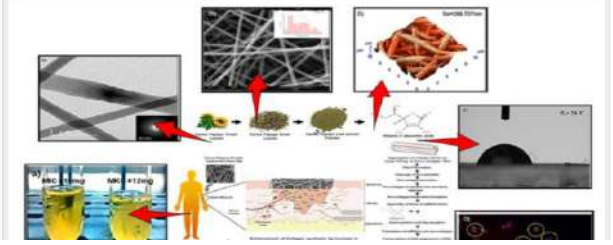
Carica papaya loaded PVA-Gelatin nanofibrous scaffold: a wound dressing material

Every year millions of people worldwide encounter mishaps that may arise from burns, surgery, accidents, or chronic diseases compromising the skin's integrity. These incidents can either result in lifelong functional impairment of the affected part of the body or may ultimately cause an individual's death due to microbial invasion and wound infection. One promising approach to promote skin regeneration is developing a nanofibrous scaffold that can mimic the native extracellular matrix and is capable of supporting cell adhesion, proliferation, and differentiation. Therefore, we have synthesized a drug-loaded nanofibrous scaffold using the electrospinning technique as a wound dressing material in the present work. The nanofibrous scaffold is used for various biomedical applications due to its ability to serve as an excellent framework for cell adhesion, proliferation, and maturation leading to new tissue formation. Our starting material choice is unique as we have blended two biodegradable polymers, namely polyvinyl alcohol (PVA), a synthetic material, with gelatin (gel), a natural polymer. Gel is a biopolymer with excellent biocompatibility, biodegradability, inexpensive, and is an excellent alternative to collagen, a major extracellular matrix component. However, it is challenging to synthesize nanofibrous scaffolds of gel alone. Also, gel suffers stability issues and has low bioavailability, which may affect the wound healing process. Therefore, PVA was used as the supporting material to develop the nanofibrous scaffold.



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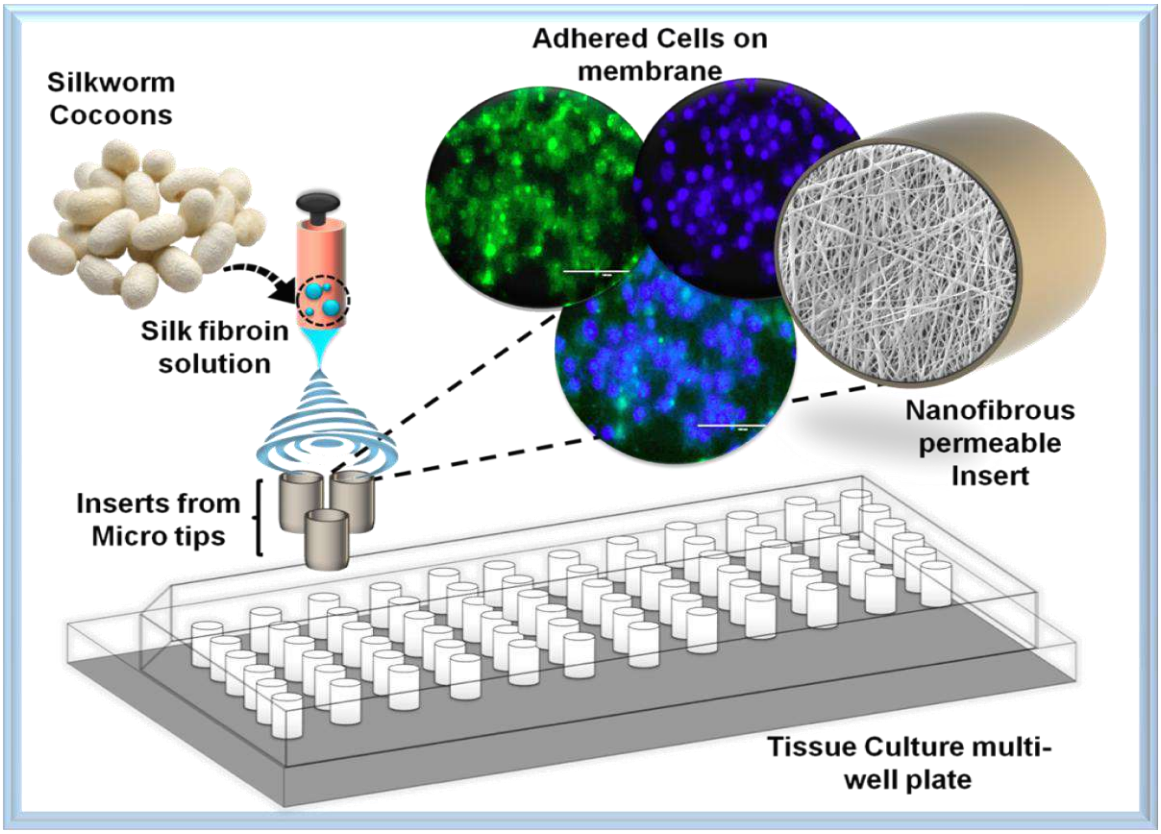
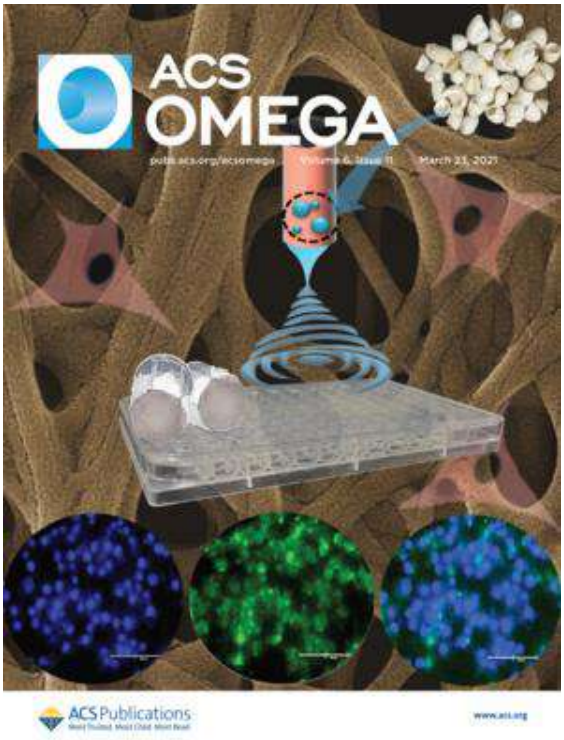
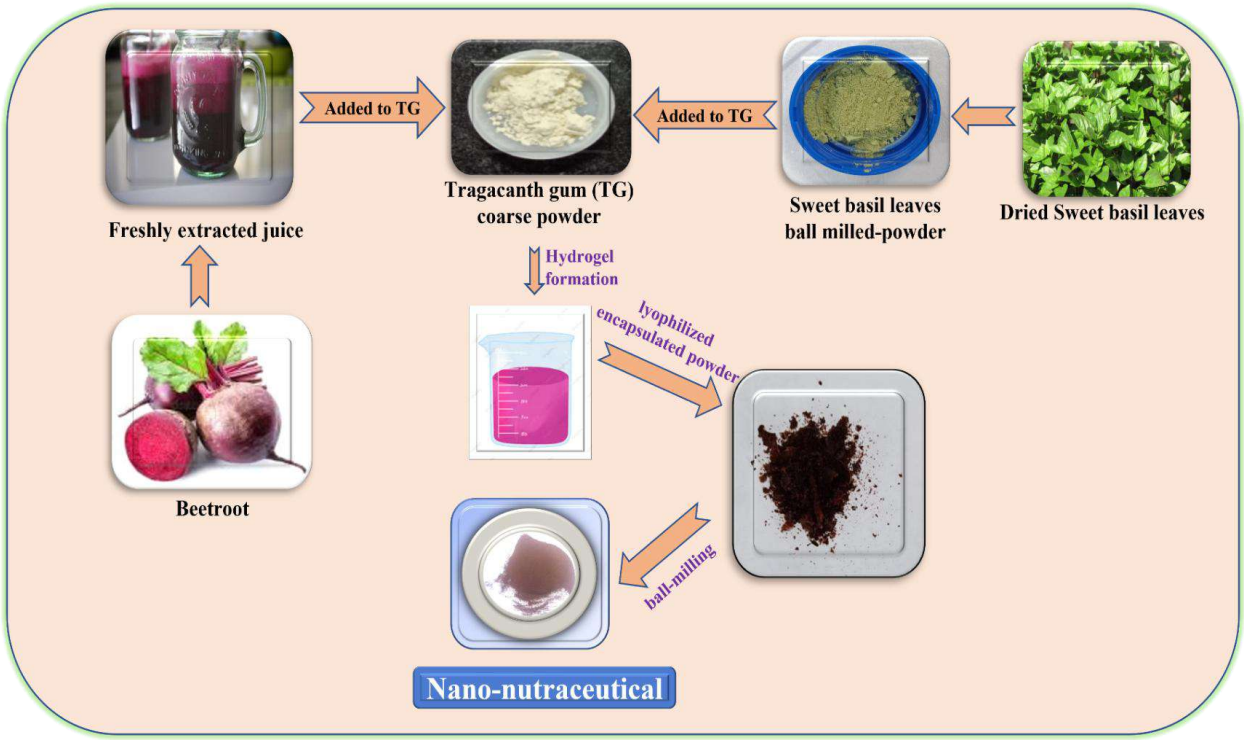
His group has also developed low cost biomaterials for bone tissue engineering and one-step fabrication of low-cost nanofibrous hanging permeable inserts for various biological applications. They have filled Indian patents for these novel technologies established by his research group.





His research group is also working on to address some of the problems relevant to food sector. They developed nano-nutraceuticals to treat anemia (filed Indian patent). Micronutrient deficiencies, such as iron, folic acid, and vitamins C and D, are currently prevalent due to inadequate consumption of natural food sources, namely raw vegetables and fruits. This deficiency is compounded by the growing reliance on synthetic nutraceuticals and processed food, which exhibit poor absorbency within the gastrointestinal tract. Scientific studies consistently indicate that naturally prepared whole foods are superior in terms of nutrient absorption compared to processed and synthetic supplements. To address this issue, we utilized FDA-approved tragacanth gum (TG) in the synthesis of nano-nutraceuticals by encapsulating beetroot juice and ball-milled sweet basil (Ocimum basilicum). TG, in its micro or macro form, possesses the remarkable ability to form hydrogels capable of absorbing water up to 50 times its weight. However, the hydrogel-forming property diminishes when TG is reduced to the nanoscale. We effectively exploited these properties to facilitate the synthesis of nano-nutraceuticals. The procedure involved encapsulating beetroot juice and sweet basil nanopowder using TG hydrogel, followed by freeze-drying. Subsequently, the freeze-dried encapsulated TG composite was subjected to ball-milling to achieve the desired nano-nutraceuticals. These nano-nutraceuticals naturally contain essential nutrients such as iron, folic acid, ascorbic acid, chlorophyll, niacin, and sugars, without the need for chemical processing or preservatives.



Recently his group has developed nano-biosensor for early detection of cancer for which an Indian patent was granted. Presently they are working with a company to develop the prototype into a product for cancer diagnosis and prognosis.

Fluorescence based cost-effective rapid diagnostic kit for detection of small cell lung cancer

In the current scenario, the dominancy of cancer is becoming a disastrous threat to the whole of mankind. Among all, small cell lung cancer (SCLC) is known for the high tendency toward early metastasis that becomes worst because of its rapid doubling rate. The prognosis of SCLC is one of the lowest among the various cancer types due to the poor availability of diagnostic tools at an early stage. Therefore, an advanced analytical approach is desired as a need of the hour for the early diagnosis to curb the menace of SCLC cancer. In this direction, the quantitative detection of cancer biomarkers with higher accuracy and sensitivity could be utilized as a remedy towards the development of an efficient platform. In the view of foregoing, the present work illustrates the significance of nano surface energy transfer (NSET) based fluorescent biosensing platform for the early stage detection of SCLC, evading the limitations of traditional diagnostic techniques. To achieve the efficient NSET phenomenon in these fluorescent biosensors, the selection of appropriate donor-acceptor pair always plays a pivotal role. For which, continuous efforts have been made towards the exploration of suitable nanomaterials possessing excellent biocompatibility along with the desired optical properties.

The proposed diagnostic kit comprises of biofunctionalized graphene quantum dots (anti-NSE/amine-N-GQDs) which act as energy donors and gold nanoparticles (AuNPs) which act as energy acceptors for the quantitative detection of neuron-specific enolase (NSE); a well-known SCLC biomarker. The functionality of the kit relies on the fundamental principle of energy transferring capability of donor species (anti-NSE/amine-N-GQDs) to the nearby acceptor species (AuNPs), followed by the recovery of fluorescence intensity on the addition of target antigen. The efficient energy transfer process has been envisaged by incorporating the optimized anti-NSE/amine-N-GQDs donor with AuNPs acceptors. The addition of different NSE antigen concentrations to the optimized donor-acceptor mixture inhibits the energy transfer process that results in the restoration of amine-N-GQDs fluorescence. Whereas, the recovery of fluorescence intensity relies on the equivalent addition of NSE antigen concentration.

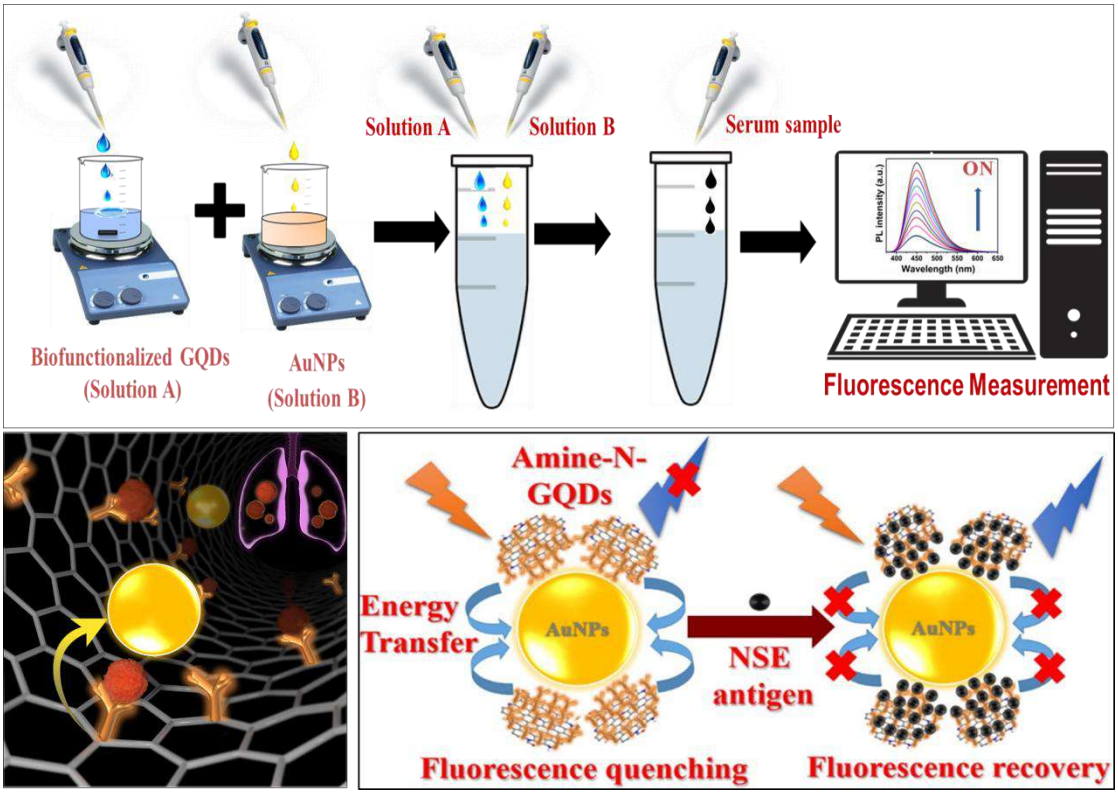


Figure 1: Schematic representation of fluorescent biosensor for small cell lung cancer detection.

In this context, the proposed fluorescent diagnostic kit successfully detected NSE biomarkers with notable biosensing parameters including a wider linear detection range (0.1 pg mL^{-1} to 1000 ng mL^{-1}), a fast response time (16 min), and a remarkable low detection limit (0.09 pg mL^{-1}). Additionally, excellent performance in real samples, with an average recovery of 94.69%.the has also been obtained.

Patent granted:

P.Gopinath, Ashish and Rangadhar Pradhan. Patent granted on 11 April 2023 for "Fluorescence based cost-effective rapid diagnostic kit for detection of small-cell lung cancer biomarker" Indian Patent Application number 202011010110.

P.Gopinath, Ashish Kalkal, Deepanshu Sharma, Ayush Tiwari and Rangadhar Pradhan. Patent granted on 28.02.2024 for MXene graphene nanohybrid thin film based electrochemical biosensors for analyte detection, its method of preparation and applications thereof" Indian Patent number 516421

(P.Gopinath)