In order of importance, list of ten best papers of the candidate, highlighting the important discoveries/contributions described in them briefly (not to exceed 3000 words)

1. G. S. Sailaja, M. Mohanty, P. V. Mohanan, T. V. Kumari, P. Ramesh and H. K. Varma, Surface phosphorylated copolymer promotes direct bone bonding, Tissue Engineering Part A, 15(10); 2009, 3061-3069

Millions of patients around undergo bone grafting/ surgical treatments annually. Commercially available PMMA based bone cement presents clinical challenges with respect to multiple types of osteolysis and implant failure due to non-osseointegration (non-bone bonding) between PMMA bone cement and host bone; hence fail to do load transfer and ultimately leading to implant failure. This work presents development of a novel surface phosphorylated copolymer of MMA and HEMA using a novel surface phosphorylation technique. Smart surface functionalization of the material essentially generate a biomimetic interface which would be cell-friendly, leading to better cell-material interactions favouring cell adhesion, anchorage, proliferation and signalling. Phosphorylation is an effective strategy to impart surface functionalization to scaffolds intended for bone regeneration. The ***simple, unique strategy of surface phosphorylation*** by phosphorous pentoxide and o-phosphoric acid that induces is a generic method that can be used for phosphorylating biomaterials containing –OH groups on its surface as such or when subjected to esterification and upon successful phosphorylation apatitic calcium phosphate would be nucleated in a biological or milieu (biomineralization- in presence of cells) or simulated physiological conditions (biomimetic mineralization), a critical event in bone tissue formation. *Uniqueness of the phosphorylation protocol developed is mainly embraced by eliminating need of any toxic solvents such as DMF, DMSO, etc*. In addition, the strategy could be adopted to various natural as well as synthetic materials (either in bulk or porous form or as nanoparticles/structures) by modulating the conditions based on the substrate characteristics. Most importantly, it is applicable in a wide temperature range from room temperature to 80^{o}C. The surface phosphorylated copolymer developed in this study invoked remarkable ***new bone formation in vivo***, validated in rabbit model as per ISO 10993. This surface phosphorylation technique has been explored for surface functionalization of several biomaterial substrates to aid biomineralization and augment bone regeneration eg: Poly (hydroxyethyl-co-methyl methacrylate) [poly(HEMA-co-MMA]- solid and porous (Tissue Engineering Part A and ACS-Biomat Sci and Eng.) (ii) Polyethylene terephthalate (PET- Mat Sci Eng C), and (iv) Polyvinyl alcohol (PVA- Acta Biomaterialia).

The key path ways associated with cellular interactions that leads to osteogeneis as a result of surface phosphorylation can indeed lead to strategic design of functional designing of bone regenerative biomaterials. Based on these findings, we have submitted a proposal to SERB, Government of India, to elucidate the signalling mechanism underlying surface phosphorylation-induced osteogenesis. The proposal has been accepted under the National Post–Doctoral Fellowship scheme – Basic Science in 2021 (File. No. PDF/2020/002685), and the work is in progress.

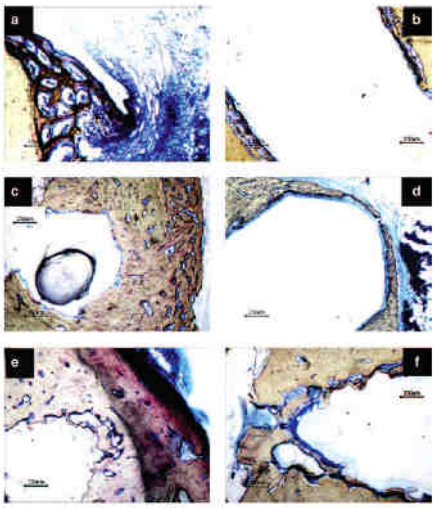
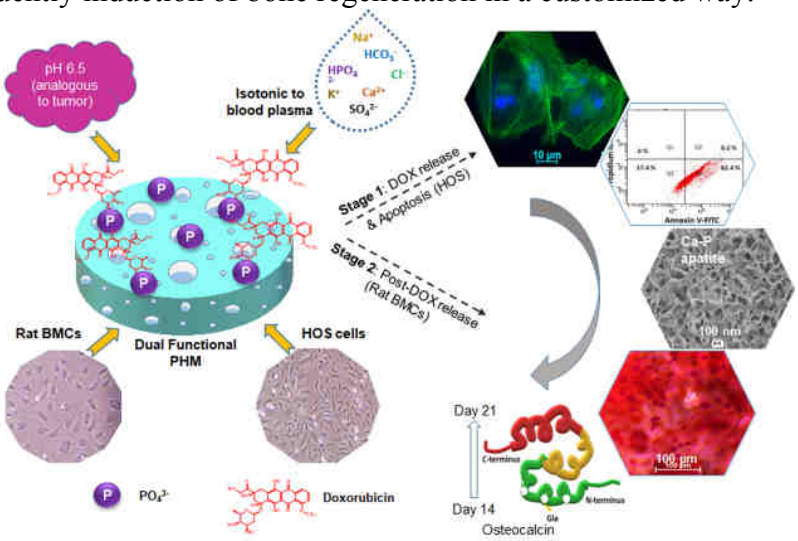


FIG. 7. Light microscopic images of the stained sections implants retrieved after 1 week (a, b), 4 weeks (c, d), and 12 weeks (e, f) surface-phosphorylated poly (HEMA-co-MMA) (a, c, e); CMW1 radiopaque PMMA bone cement (control) (b, d, f). PMMA, poly (methyl methacrylate).Color images available online at www .liebertonline.com/ten.

2. S. Sreeja, P. Ramesh, P. R. Harikrishna Varma, G.S. Sailaja*, Hierarchically porous osteoinductive Poly(hydroxyethyl methacrylate-co-methyl methacrylate) scaffold with sustined Doxorubicin delivery for consolidated osteosarcoma treatment and bone defect repair', ACS Biomaterials science and engineering, 2021, 7, 2, 701–717

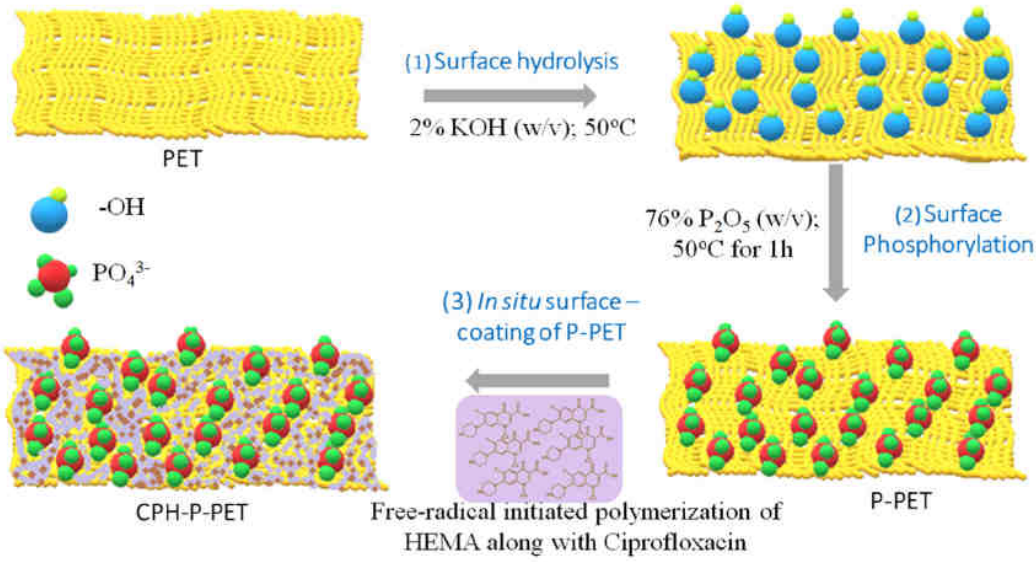
A bi-front therapeutic approach for osteosarcoma is presented this study. Surface-phosphorylated hierarchically porous hydrophilic therapeutic scaffold [Doxorubicin-loaded poly(HEMA-co-MMA)] was developed to present a comprehensive therapeutic approach for osteosarcoma that performs two active roles - pH-responsive sustained chemotherapeutic drug release followed by inherent bone formation and (*kindly see the schematic representation below*). In addition, it also induces apoptosis of Human Osteosarcoma (HOS) cells by establishing drug delivery and thereby tumour cell annihilation. Most importantly, inducing biomimetic mineralization successive to sustained DOX-release emphasizes its functionality as a bi-faceted treatment system for osteosarcoma. Hence, the scaffold presented would be a promising therapeutic strategy against osteosarcoma by the localized chemotherapeutic drug delivery subsequently induction of bone regeneration in a customized way.



Schematic illustration depicting the functionality of surface-functionalized poly(HEMA-co-MMA)

3. S. Sreeja, C.V. Muraleedharan, H.K.Varma, G.S. Sailaja *, Surface transformed osteoinductive polyethylene terephthalate scaffold as a dual system for bone tissue regeneration, Materials Science and Engineering C, 109, 2020

The surface-phosphorylated wet-spun PET fibrous matrix coated with ciprofloxacin-impregnated biodegradable polymer, serves as a dual therapeutic scaffold that exhibited high bactericidal activity and osteogenic potential.The dual functional surface-transformed PET scaffold [Ciprofloxacin-impregnated HEMA coated phosphorylated PET (CPH-P-PET)] was designed to address bone infection and provide a platform for repairing and regenerating damaged bone (*kindly refer to the schematic representation below*). The CPH-P-PET also served as an excellent antibiotic delivery vehicle based on the cumulative release profile of ciprofloxacin. *In vitro* calcium phosphate apatite formation and other biofunctional assays depict its proficiency in new bone formation. Furthermore, confirmative evidence from the expression of osteogenic biomarkers – Alkaline phosphatase (ALP) and Osteocalcin (OSN) - in rat Bone marrow Mesenchymal Cells (BMCs) elucidated the osteoinductive nature of the scaffold. Altogether, the antibiotic carrying surface-transformed PET is an excellent dual-functional scaffold for bone regeneration and prohibits bone-specific infections.



Scheme 1. Fabrication of dual functioning CPH-P-PET system.

4. G. S. Sailaja, Balagopal. N. Nair, Julian D. Gale and Yamaguchi; Amino acid inspired microscale organization of metallic nanocrystals; J. Mater. Chem. A, 2014, 2, 100-106

Amino acid inspired micro-scale organization of platinum and silver nanocrystals and the complementary oligomerization of amino acids is reported in this study. The spatial organization of the microstructures is highly species specific with unique morphologies corresponding to particular combinations of a metal–amino acid system. Alanine, glycine and glutamic acid were used to illustrate the concept. The presence of a poly(amino acid) or stabilizing agent alters the size and configuration of the microscale assembly. The molecular interaction between Pt and amino acid as well as the synthesis conditions play key roles in

dictating the final shape of 3D assembled structures. The protocol offers a very facile strategy for designing diverse molecular building blocks of metallic microstructures for advanced applications by choosing versatile combinations of metal-ions and amino acids. Platinum integrated structures, in addition to their diverse architecture, showed good stability at high temperatures. The highlight of this invention is that it paves the way for designing various metal-amino acid conjugated structures towards diverse nano and biomedical applications. ***This investigation has led to three Japanes patents as well. Exploring this work we have later developed new protocol for making super paramagnetic iron oxide (SPION) with high saturation magnetization (78emu/g) and high magnetic hyperthermia potential and is highly biocompatible and uptaken by cells (New Journal of Chemistry, 2020)***

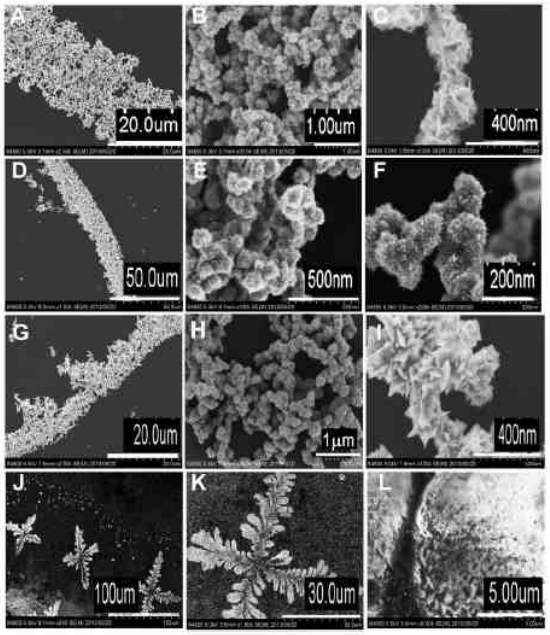


Fig. 1 Morphology of different types of Pt–amino acid molecular building blocks and their micro-scale assembly formed under stirring conditions. (A–C) Pt–alanine; (D–F) glycine; (G–I) glutamic acid; and (J–L) poly(glutamic acid).

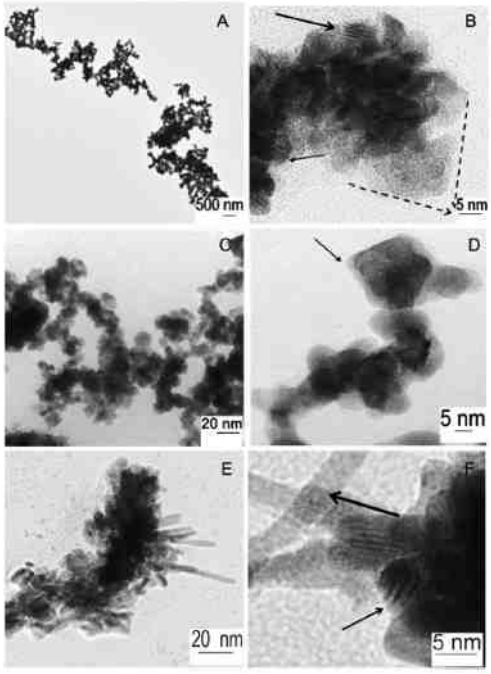
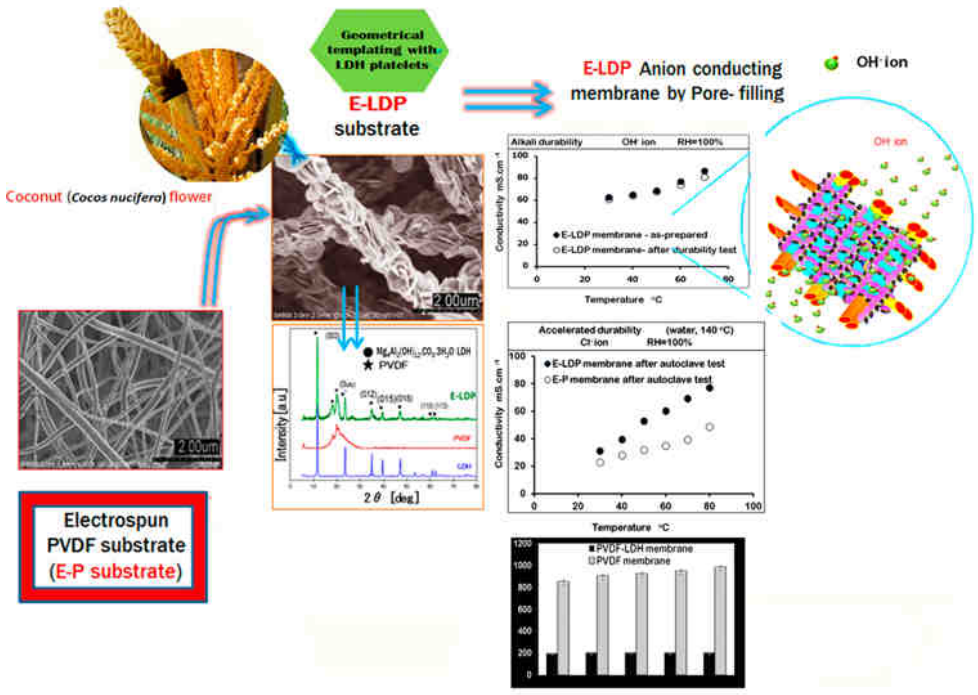


Fig. 4 TEM images of different types of Pt–amino acid molecular building blocks formed under stirring conditions. (A and B) Pt–alanine; (C and D) glycine; and (E and F) glutamic acid.

5. G. S. Sailaja, P. Zhang, G. M. Anilkumar, T. Yamaguchi, Anisotropically organised LDH on PVDF: A geometrically templated electrospun substrate for advanced anion conducting membranes, ACS Appl. Mater Interfaces, 2015, 7 (12), pp 6397-6401

Organic-inorganic hybrid porous substrates have recently been used in a number of applications such as separators in batteries, fuel cell electrolyte membrane substrates, and electrode materials for supercapacitors. Among the several fabrication methods adopted including phase-inversion and template-assisted techniques, electrospinning has acquired remarkable interest because of its superior 3D interconnecting configurations, high surface area, and rich variety of morphology. Nevertheless, their special nonwoven structure, larger pore size (~ 2 μ m), and poor wettability remain as unresolved challenges, restricting their

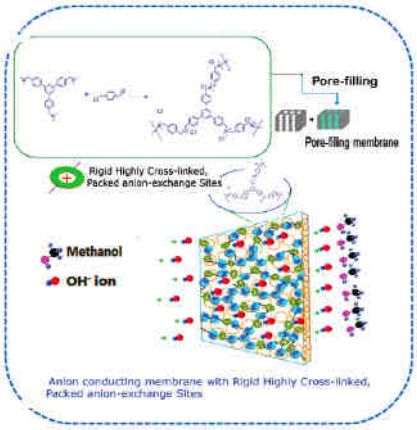
applications mainly to milder environments. A bioinspired geometric templating of an electrospun PVDF substrate with hexagonal platelets of Mg-Al layered double hydroxide (LDH), an intrinsic anion conductor, is developed. The distinctive morphology restructures the internal pore geometry and modulates the dynamic wetting profile of PVDF, transforming it into a highly functional substrate for Solid state alkaline fuel cells (SAFC) anion conducting membranes. The membrane fabricated with PVDF-LDH substrate exhibited exceptionally high durability (>140°C), high anionic conductivity, ion exchange capacity (IEC), restricted swelling, and improved tensile strength, overcoming critical challenges associated with PVDF electrospun substrates and validating its immense potential as a high temperature- stable and durable substrate for advanced fuel cell membrane applications. ***The findings in this work has led to a Japanese patent,***



6. G. S. Sailaja, S. Miyanishi, T. Yamaguchi, A durable anion-conducting membrane with packed anion-exchange sites and an aromatic backbone for solid-state alkaline fuel cells, Polymer Chemistry, 2015,7964-7973

Contemporary design strategies aimed at developing highly functional anion conducting membranes (ACMs) for solid state alkaline fuel cell (SAFC) applications are often hampered by intrinsic limitations such as less efficiency in controlling swelling, declined alkaline durability, high fuel cross-over and/or poor stability against OH radicals especially for polyelectrolytes composed of aliphatic chains. Hence, it is a challenging task to develop an ACM that satisfies all pre-requisites: high conductivity, alkaline durability, chemical stability and very low fuel cross-over for successful SAFC applications. This work presents the systematic design of a simple molecular architecture based on the benzyl ammonium group and benzene without a hetero atom segment as a promising alkaline durable ACM with high

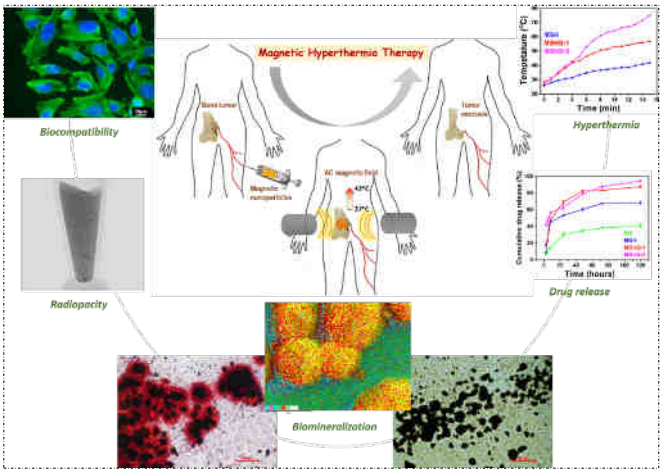
anion conductivity. We have designed a new monomer 1,3,5-tri[p-(N',N''-dimethylaminomethyl) phenyl]benzene (TDAMPB) with three tertiary amino groups that generates poly-TDAMPB (PTDAMPB) with three anion exchange sites per molecule upon in situ cross-linking. This highly cross-linked aromatic polyelectrolyte could generate highly packed anion-exchange sites by polymerization in the pores of a porous substrate and thereby presents an imperative solution for the existing challenges associated with current SAFC membranes. The PTDAMPB membrane performances were compared with an aliphatic poly(vinylbenzyltrimethyl ammonium chloride) (PVBTAC) membrane. The results demonstrate that the PTDAMPB membrane exhibited high OH^- ion conductivity similar to PVBTAC membranes, but exceptionally low methanol permeability and low swelling while maintaining good durability against hot alkali, boiling water and oxidative decomposition in contrast to PVBTAC. The functionalities of the PTDAMPB membrane satisfy the anticipated requirements for a viable SAFC, which is difficult to attain simultaneously for a conventional anionconducting membrane and hence the results of this work address a major unresolved challenge representing an advancement toward successful SAFC applications.



7. K.R. Sneha, S.Sreeja, G.S. Sailaja*, Radiopacity endowed magnetic nanocomposite with hyperthermia and in vitro mineralization potential: a combinatorial therapeutic system for osteosarcoma, Biomed. Mater, 16(4). 2021, doi: 10.1088/1748-605X/ac01af

Osteosarcoma is the most common primary **bone cancer** occurring in children as well as adolescents. Contemporary treatment modalities like surgical tumour resection, hormone therapy, chemotherapy and radiotherapy are inefficient in improving the survival rate of osteosarcoma patients. Superior alternatives like hyperthermia, photodynamic therapy and low/high-intensity pulsed ultrasound sonodynamic therapy exhibited enhanced cure rates and hence they are in the limelight recently. when therapeutic materials are having imaging competencies they are termed as 'theranostic' materials; which completely eliminate the need of two separate systems to fulfill two distinct objectives of therapy and imaging. 'Nanotheranostics' is specific to the development of nanomaterials possessing theranostic potential. The widely used diagnostic methods in nanotheranostics include Computed tomography (CT), Magnetic Resonance Imaging (MRI), Positron emission tomography (PET), Single photon emission computed tomography (SPECT), Optical imaging etc.

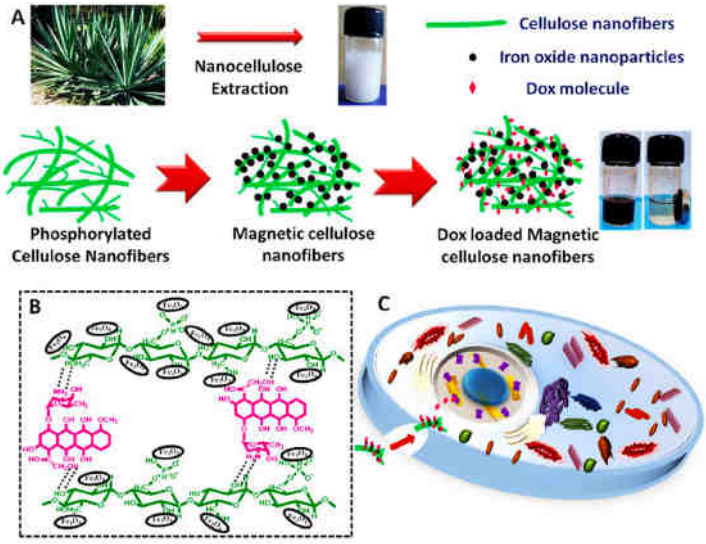
This work developed a multifunctional theranostic platform for osteosarcoma. The multifunctional magnetic nanocomposite composed of maghemite, strontium doped hydroxyapatite and silica nanoparticles prospectively holding indispensable therapeutic features such as ***magnetic hyperthermia, in vitro biomineralization, sustained drug release and intrinsic radiopacity*** is developed for the treatment of osteosarcoma by conventional sol-gel technique. Remarkably, all functionalities of the individual components were preserved in the magnetic nanocomposite. Thus sustained drug delivery of droxorubicin, magnetic hyperthermia for treatment, radiopacity and bone regeneration potential for imaging, easy monitoring and bone regeneration etc. are combined in a single platform (S*aturation magnetization of 47.4 emu* g^{-1} ; *hyperthermia temperature (42* ^{o}*C) at a very low exposure time of 4 min;* exceptional x-ray attenuation ability (*contrast enhancement 154.5% in digital radiography; CT number 3100 HU), early biomimetic mineralization* (*in vitro*) evident by the formation of spheroidal apatite layer (*Ca/P ratio 1.33*) harvested from FESEM–EDX analysis and controlled release of *Doxorubicin, the clinically used chemotherapeutic drug: 87.7% at 120 h* in tumour analogous pH (6.5) when compared to physiological pH (71.3% at 7.4). MTT assay complemented with cytoskeleton (F-actin) staining of human osteosarcoma (HOS) cells affirm biocompatibility of MSHSr1. *In vitro biomineralization authenticated by Alizarin red S and von Kossa staining* has been further corroborated by semi-quantitative calcium estimation of HOS cells cultured with MSHSr1 for two weeks. The results therefore validate the multifunctionality of MSHSr1 as a combinatorial therapeutic nanocomposite for osteosarcoma treatment.



8. N. S. Sumitha, S. Sreeja, P. J. G. Varghese, G. S. Sailaja, A dual functional superparamagnetic system with pH-dependent drug release and hyperthermia potential for chemotherapeutic applications, Materials Chemistry and Physics, Volume 273, 15 November 2021,https://doi.org/10.1016/j.matchemphys.2021.125108

In this study, a novel platform that combines magnetic hyperthermia and targeted drug delivery aspects to enhance the efficacy and to reduce the side effects of non-targeted chemotherapeutic drug delivery in cancer is developed. This dual functional nano platform is synthesized from phosphorylated nanocellulose and superparamagnetic iron oxide nanoparticles (SPIONs). To

make this specifically targeted to cancer cells. It was designed to be pH responsive so that at drug release happens preferably at pH, analogous to tumor microenvironment.



9. Praseetha R. Nair, S.Sreeja and G.S.Sailaja*, In vitro Biomineralization and Osteogenesis of Cissus quadrangularis Stem Extracts: An Osteogenic Regulator for Bone Tissue engineering, Journal of Biosciences, volume 46, 2021

Contemporary demand calls for a high restorative index as an indispensable requirement for bone tissue engineering scaffolds, where therapeutic agents of natural origin function as a modulator for new bone formation become of utmost importance. This study systematically investigated the edible stem part of *Cissus quadrangularis* (CQ) *Linn* as a natural resource of bioactive metabolites capable of invoking early biomineralization and osteogenesis. Sequential extraction of CQ stem (n-hexane\chloroform\ethyl acetate\methanol\water: Phytochemical screening of the extracts: hexane extract (HE), chloroform extract (CE), ethyl acetate extract (EE), methanol extract (ME) and aqueous extract (WE) by qualitative and quantitative assays, UV-Visible and FTIR spectroscopic analyses. Cytocompatibility and proliferation index of the extracts and their effect on cellular architecture were investigated by MTT assay and F-actin/DAPI staining, respectively, in Human Osteosarcoma (HOS) cells. Aqueous extracts (WE) and hexane extracts (HE) were found to have significant osteogenic potential. This was evident from the expression of alkaline phosphatase as early as 7 days in cells treated with WE and HE. Configuring abundance of bone regenerative phytochemicals in HE and WE, this work in fact present ample opportunities for customized bone tissue engineering and development of a completely bioresorbable bone regenerative scaffold of natural origin.

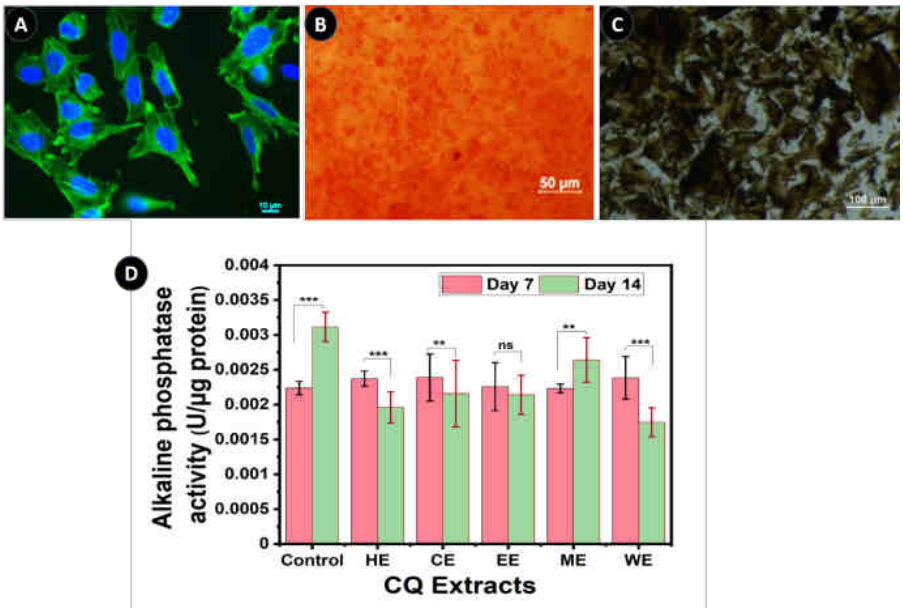


Figure 1. Cytocompatibility and biofunctional evaluation of CQ extract. A, B and C represents cytoskeleton staining, ARS and von-kossa staining of HE extracts whereas D represent Alkaline phosphatase activity of HE extracts in HOS cells.

10. Ananjana K, Swetha S, P. Prakash, Nishad T, M. Komath, B.N.Nair and **G.S. Sailaja ***., Amino acid inspired tunable superparamagnetic iron oxide (SPION) nanostructures with high magnetic hyperthermia potential for biofunctional applications, **New Journal of Chemistry**,2020, DOI: 10.1039/C9NJ05343C

A novel room temperature synthesis protocol has been developed for the synthesis of Superparamagnetic iron oxide nanoparticles (SPIONs), having high saturation magnetization (Ms 78 emu/g). These SPIONs are biocompatible and can be magnetically targeted to tumour site, uptaken by tumour cells, capable of generating intracellular heat (temperature of 42 $^{\circ}$C–45 $^{\circ}$C) upon induction of alternating magnetic field which is sufficient to induce tumour necrosis, locally keeping the healthy normal cells/tissue intact.

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