|| Volume 6 || Issue 8 || August 2021 || ISSN (Online) 2456-0774
INTERNATIONAL JOURNAL OF ADVANCE SCIENTIFIC RESEARCH AND ENGINEERING TRENDS

FUNCTIONAL POLYMERIC MATERIALS AND THEIR BIOMEDICAL APPLICATIONS: AN OVERVIEW

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Abstract- Due to technological advancement and population growth, the use of synthetic plastic materials increases day by day, which not only a threat to us, but also the whole biological community. Hence, scientist and researchers are focusing on new polymer and composite materials, which are compatible with various applications ranging from issues related to electronics, packaging and advanced medical applications used in our day to day life. This review mainly focused on fabrication methods of biobased polymer composites and nanocomposites mainly melt-extrusion, electrospinning, solution mixing, in situ methods and latex technology. Especially, more attention is drawn towards the field of biomedical applications which mainly includes tissue engineering including skin, oral tissues, blood vessels and bone, wound dressing and dental resin-based biocomposites.

Keywords: Polymer composites, electrospinning technique, tissue engineering, wound dressing

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I. INTRODUCTION

The global environmental concern demands the least use of petroleum based product maetrials and more attaination is given for sustainable and eco-friendly pollution free surrounding, which demands the design and development of environmentally friendly functional materials for various sectors[1]. Development of high performance materials at reasonable cost and eco-friendly approach is the basic challenge for the industries and researchers throughout the world. The problems related to the petroleum based products can be solved by using more renewable resources. The wide use of plastics on health sector, automotive, packaging and electronic industries fulfils the needs of modern society, but, however these products are disposed rapidly and these huge amounts of plastics really became a threaten for our ecosystem. To restrict the use of plastic and protect our environment, biodegradable polymers are the only alternative choice to replace the conventional polymers. Althouth is is sustainable and beneficial to our society, but still possesess many disadvantages, which drag out back to the polymer industry. Composite is a substance, which may contain either two or more distinguishable components that combiningly function together in a better way to attain improved properties. In general composites involve two different phases i.e. a matrix phase and a dispersed phase. The use of composites increased at a surprising rate, because of some unique properties such as light weight, durability, corrosion resistant, high fracture resistance, high impact and flexural strength, good surface finishing, cost effective etc. [2] A good composite is characterized by their homogeneity and controlled distribution of filler maetrials over the matrix phase. Polymer biocomposite is a material having matrices such as polymers, biopolymers and natural fibers, clay or any other natural substances as reinforcing materials. Polymer composites are progressively gaining importance as supernumerary materials for metals and ceramics in many applications in different fields such as aerospace, automotive, marine, transportion, packaging and electronic, but now a day it is more effectively applied in biomedical fields and as implant maetrilas of various designs in tissue engineering and manufacturing of artificial body parts, because of its property of biocompatibility, biodegradability and bioactivity and non-toxicity. The major objective of this work is to focus the benefits of attractive property of composites of polymeric material in modern medical applications associated with various technologies for synthesis. The features of the functional polymeric composites depend on the nature of the chemical functional groups present on the backbone chains. These modified features of improving some properties such as mechanical strength, enhanced compatibility, flexibility, reactivity to processability and chemical stability. Functionalization of polymers may lead to “smart materials”.

Polymers can also be functionalized by copolymerization with other monomers to improve the advanced useful propertie. [3]

2. Classification of Composites

Depending upon the suitability of the matrix phase,the classification of the composites is reported as Ceramic matrix composites (CMCs), Polymer matrix composites (PMCs),Metal matrix composites (MMCs). Based upon reinforcement, composites are classified as Particulate, Laminate and Fibrous composites. Fibrous are categorized into Natural biofibres and Synthetic Fibres. Biofibre composites can be allocated into two categories: - Degradable and non-biodegradable matrixes. The composites of polymer that are manufactured from bio-polymers as the matrix and fibers of natural origin as reinforcing materials are commonly called as green composites. The green composite materials are now considered as a new generation material of sustainable composite and when it combines with fibers and resins of natural origin, the product obtained becomes lighter, stronger, recyclable and easily biodegradable. [4] Here, we will illuminate completely the functional composite materials, including their process of fabrication and applications in medical field. Figure-1 shows the different grouping of the composite materials.

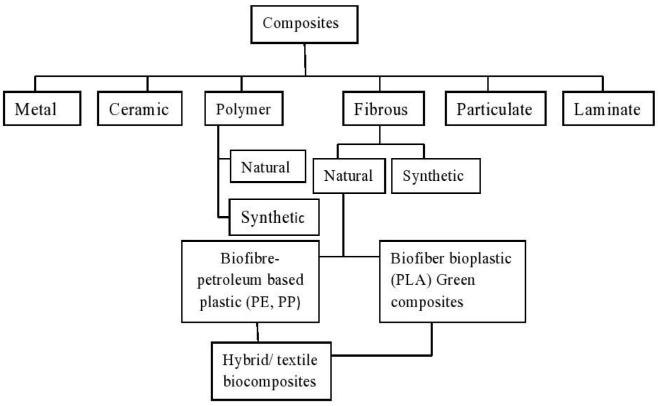

Fig. 1 Classification of composites

3. Processing technology of various polymer composites

Becacuse of simple methods to manufacture and less expensive the polymer matrix composites (PMCs) are very popular and widely applied in varios important fields. Polylactic acid, polyarylic acid and copolymers of polyglycolide and polylactic acid are used effectively in various biomedical applications. Polymers without a reinforced component exhibit poor properties, but by reinforcing the filler materials, its properties are increased in a amazing rate [5]. Fabrication of PMCs is done by reinforcing fibrous component with the polymers, which permits the following characteristics:

a) More specific stiffness

b) Greater specific strength

c) Good abrasion resistance

d) High breakage resistance

e) High impact resistance

f) Good fatigue resistance

g) Good resistance to corrosion

h) Low cost and easy fabricabilitty

3.1. Electrospinning

The process electrospinning techniques usually carried out by using the fibers with diameter ranging from 2 nanometres to some micrometres by applying high voltage electiicty. In spite of common spinning techniques, electrospinning techniques are preferred because this could process nanofibers with large surface area. [6] Electrospinnig system basically consists of syringe pump, high-voltage power supply, rotating drum. The two normal categories of electrospinning are horizontal and vertical sets. The solution of the components is placed in a syringe attached with a stainless steel needle. The solution will be then moved towards the collector of varinging charged. At a particular direct current (DC), the electrical forces of repulsion is exceeded the surface tension of the solution of the polymeric material. Then, after that an electrified jet will be produced from the tip of the Tylor cone and the evaporation of the solvent will be initiated with the formation of electrospun Nano fibrous membranes [7]. Figure-2 shows electrospinning method for synthesis of functional composites.

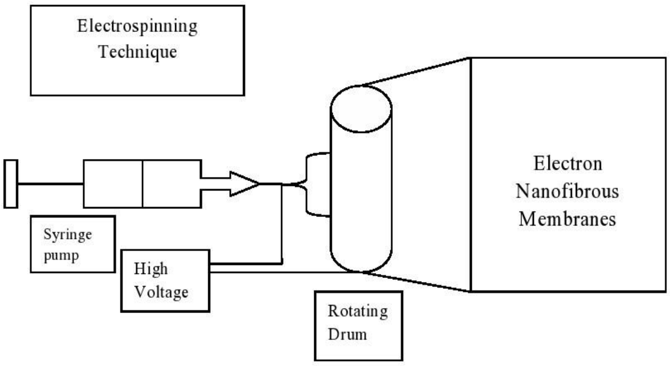

Fig. 2 Electrospinning Technique for synthesis of polymer composite

3.2 Melt-Extrusion

One of the most common and popular technique adopted in order to fabricate polymer composites is melt extrusion. This technique is commonly used by addition of the plasticizer to the extruder. In this technique polymers and fillers are mixed using a twin screw extruder at a particular temperature for a certain time period. When extrusion is completed, under certain conditions, polymer composites are shaped by using compression molding to get the final product. By varying the filler content the mechanical and thermal properties of the prepared composites can be controlled. Use of dry nanocellulose during the process of extrusion is difficult as it forms hydrogen bonds in amorphous state, undergoes aggregation and difficult to disperse. In some synthesis over melt extrusion, wet extrusion is preferred due to lower range of temperature and is appropriate for applications in biomedical field . The protein can be easily degraded due to higher temperature of the melt extrusion. For instance, PLA pellets having different % of weight of ceramic powder were blended separately using microcompounder along with the conical screws of less capacity under inert nitrogen atmosphere shows better result. To obtain PLA reinforced ceramic bioresorbable composites, simultaneously, a set of various rotation speeds of the screw such as 150, 200, and 250 rpm, residence time 1–4 minutes and temperatures (200 and 205 °C) were mainatined. By blended 97% of low-density polyethylene (LDPE) with 3% of Titania, halloysite and carbon nanotubes using a brabender plastograph EC batch mixer functioning for about 7 min at temperature of 180 °C, where a new novel composite having excellent corrosion resistance is obtained [8, 9].

3.3 Latex Technology

Polymer network can be incorporated using conductive fillers by latex technology to produce conductive polymer composites. Some advantages in this process includes easy processing, homogeneously dispersed fillers, process upscaling and filler materials are homogeneously distributed in the polymer matrix. Using this technique nanofiller materials can be inserted into a excessive viscous form of polymermatrix. Using this technique, the 3D framework of the particles of filler materials have been created in galleries of the polymer. Latex technology normally carried out in three steps

- The distribution of nanofillers in colloidal form
- Combination with the latex of polymeric materials
- Proper drying of the colloidal form of mixture

The polymer composites having graphene and carbon nanotubes as filler materials can be successfully synthesizd by using this technique, which may be utilized in various medical applications [10].

3.4 In Situ Process

In the *in situ* process of polymerization process, filler materials at first swollen along with the liquid monomer, then asuitable initiator is incorporated by using heat or radiation, which initiates the process of polymerization. The process of *in-situ* polymerization is adopted in order to fill the interlayer in between the nanolayers along with the monomers, stimulating the process of polymerization between the space of the layers. The amont of solute present the solution identifies the the rate of dispersion of the polymer and the mixing method and time determines the uniformity. Filler maetrials normally graphene or its modified form can be swollen before absorption. Using this process, high % of CNT with functional composites can be easily processed, which can be further diluted by other techniques. Nanoclays are excellently embedded in the space of inner layer of the silicate depriving dropping off [11].

4. Applications of the Polymer Composites in Biomedical Field

Functional Polymer composite materials have bben proved its promising potential in the field of biomedical applications, including cancer therapy, tissue engineering, dental therapy, wound dressing, blood vessels, oral tissues, bone transplantation, where their versatility is clearly visible. Most of the industries using advanced technique are targeting to fulfil these necessities by using these novel, environmentally friendly and reliable polymer composites [12].

4.1 Application in Tissue Engineering

The objectives of the tissue engineering is to replace or repair damaged or injured tissues or to synthsize artificial tissues for transplantation during the surgical process, which is preferred upon the failure of physiologic reaction using a scaffold biomaterials which acts as a template to promote the growth of cells and generation of new cells. Biomaterial scaffolds can be synthesized from various organic and inorganic polymers including synthetic and natural origin. In addition to cell proliferation and adhesion to tissue and organ reconstruction, polymer composites propmotes the growth of the cells, migrate and seed. Scaffolds must be biocompatible, suitable surface chemistry, appropriate pore size, morphology to promote cellular functions, good mechanical strength, etc. Scaffolds mustfunctions as agents of drug delivery for the growth factors, antibiotics and chemotherapeutic agents, which depends on the nature and kind of the tissue to be renovated or repaired. A strategy of TE is schematically shown in the figurew-2. 3D polymer-based scaffolds are promising materials for simulation of native morphology. Thin films of biocompatible protein polymer have beensynthesized for utilization in the implantable devices. The two major standards of employing 3D scaffolds are autografts and allografts, which may include some limitations, autograft may cause donor –site morbidity and allograft have high risk of disease transmission [13, 14].

4.2. Bone Replacement

Bone of the skeletal system consists of collagen fibers along with nanocrystals of hydroxyapatite(HA) , blood vessels, cells and mucopolysaccharides. 70% by weight of the dry bone is covered by HA mineral, which is responsible for the stiffness of bone. Collagen fibres in bone is aligned along with the main stress direction and have low elastic modulus. Fracture is treated as one of the usual problems associated with bone structure, location, crack volume and orientation. Implants are temporarily placed inside the body and can be eliminated after recovery. A numer of degradable polymeric maetrials, either synthetic origin or natural origin such as poly(propylene fumarate), Chitosan, polyesters, and copolymer poly(lactide-co-glycolide) (PLAGA) can be utilized as a suitable scaffold systems for reparing of bone tissue. The *in situ* preparation of scaffolds of PLAGA/$Ca_3(PO_4)_2$ microspheres were gestated in simulated body fluid (SBF) for few weeks and theorized that a 20% drop in molecular weight scaffolds occurred over 8 weeks. Also pH of the scaffolds of the biomaterials (SBM) is decreased, due to the dissolution of calcium phosphate. It has been hypothesized that the free Ca^{2+} content in the SBF containing scaffolds, first increased from 20% to 40% in 4hr of the incubation period and then, again declined to 40%, indicating a massive release of Ca^{2+} ions interlinked with reprecipitation on the surface of the scaffold. But, however frameworks of these composite materails instigated reprecipitation of $Ca_3(PO4)_2$ for a bone implant incorporation method [15, 16].

PLA is frabicated through the bioglass fibre (BGF) and treated with air plasma to improve the mechanical and biological performance and made it a suitable material for weight bearing fixations i.e. long bone fractures (for design bone plates). These composites kept in plasma exposure over 30s and found around 13.5%, 31% and 33% increase in flexural strength, tensile strength and interlaminar shear strength respectively. Also, the better interaction in between the network of PLA matrix and fibers, which was evidenced by the failure shifting to the PLA. As a result of this, bone-like layers of calcium phosphate were set up at the surface of the disintegrated fibers, which is necessary for bone repairing processes. In addition to this process, the strength and toughness, many biometallic polymeric composites applied for the internal fixation methods. The rod like shape is synthesized by using the composite material based on PLA on combination with Mg by using the technique of injection molding (PIM) and highly effective for fixation of bone fracture . Scaffolds of PLA/ethyl cellulose (EC) /HA have been studied as weight-bearing alternative material and exhiibts excellent result in tissue engineering . The results discovered that the compressive yield strength, weight loss, porosity, and contact angle, after 8 weeks were 1.57 ± 0.09 MPa, 4.77 ± 0.32%, 84.28 ± 7.04%, and 45.13 ± 2.40°, respectively. Recently, for bone tissue engineering polymer and copolymer are blended with Hydroxy Apatite (HA), Chitosan (CS) and Alginates to form bioactive, biocompatible bone scaffolds for improving their instability, mechanical weakness, shape retention property, cell adhesion and growth [17, 18].

4.3 Application in Blood vessels

In the repair or formation of new blood vessels, the vasucal regeneration is a major challenge for the pateints who suffers coronary artery and peripheral vascular bypass surgery. One of the promising potential of functional polymer composites for biomedical application is combination of synthetic vascular grafts with tissue engineering vascular grafts in order to repair or replace the injured or damaged vessels. Electrospinning technique is commonly used for designing 2D and 3D fibres using artificial and natural polymers which are used for processing vascular grafts. It has been reported that bacterial nanocellulose(BNC) containing β-1,4 linked D-Glucose dimers have some excellent properties such as excellent water holding capacity, ultrafine nanofiber matrix, good crystallinity, biocompatibility, chemical purity, tensile strength. It was reported that BNC composite blended with PVC can be evaluated as artificial blood vessels. These fabricated composites have a good check on the tensile and water permeability characteristics. By controlling the BNC content the mechanical characteristics of these composite maetrials can be controlled. [19, 20]. The mechanical characteristics of the synthesized composite materials were controlled and regulated by the content of BNC tube. Normally two different kinds of tubular bioreactors were utilized in the processing application of BNC tubes of appropriate diameters. The tubes assembled from the first bioreactor was a silicone tube of about 60 mm diameter and a glass tube, were defined as S-BNC tubes. The other bioreactor present synthesizes two silicone tubes having various calibers, which were termed as D-BNC tubes. The D-BNC/PVA composite shown a high tensile strength whereas the composite of S-BNC/PVA have relatively lower tensile strength. This synthesis facilitaes transplantation of veins and artery. Figure-3 shows the propagation of pig iliac endothelium cells (PIECs) on coverslips, BNC/PVA composite tubes, BNC tubes, and PVA tubes at 1,3,5 and 7 days after cell seeding. Recently, chitosan/gelatin bilayered composites is developed and tried to mimic the tensile strength and structural properties of macroporous blood vessels, biological blood vessels, which exhibited a large surface area for cell adhesion and proliferation. These macroporous layer are biodegradable with time, which was was established by fibroblast cell proliferation on the fabricated frameworks. Due to amazing mechanical characteristyics and low degradability of some synthetic polymeric maetrials such as PLA, polycaprolactone (PCL) and poly(lactic-co-glycolic) acid (PLGA), can be utilized as encouraging scaffolds for building of cardiac tissue. The PCL blended with gelatin can be used to process the fibers of the composite with enhaced cell–matrix interactions as scaffolds of blood vessel. The water absorbency of PCL fibers was improved from hydrophobic to hydrophilic nature, when gelatin is gradually incorporated in it. The presence of incorporation of gelatin significantly affects the crystallinity and thermal resistivity of the scaffolds. The high % of gelatin suppressed crystallinity and retads the tensile strength of the scaffolds. Whereas, scaffolds of 100% PCL, 70% PCL:30% gelatin favours the tensile behaviour of human coronary arteries [21, 22].

4.4. Skin Treatment

Skin is the first protective barrier of human body against harmful pathogens, antigens and considered to be the vital part of our body. When skin is exposed to several injuries such as serious burns, skin tissues were affected by various infections, damage and necrosis, which are not self-repaired. Skin regeneration requires biodegradable and biocompatible materials, which is now becoming one of the major challenges in the field of medical science. Various skin scaffolds are synthesized, which required to mimic the features of natural extracellular matrix (ECM). Although polymeric nanofibres possess various special features, such as high surface to volume ratio, better mechanical strength, high water absorbance capability, these maetrials can be used as carriers for antifungal, antibiotic, anticancer drug molecules. Several natural and synthetic polymer based hydrogels are fabricated using as collagen, alginate, chitosan, hyaluronic acid (HA), PVA and polyethylene glycol. .The material for skin regeneration and also proliferation obtained by electrospinning of chondroitin sulphate and modified HA. Also, thin films of alginate were produced and used for healing of burned and injured skin [23, 24].

4.5. Wound dressing

Wound dressing and healing is a cellular and molecular process, which includes treatment of damaged skin tissues, blood loss, microbial infections, physical protection etc. Specifically in this process fibroblasts are shifted to the affected portion and forms the collagen fibers belonging to the extracellular matrix, which supports the proliferation and survival of keratinocytes. Wound dressings needs active materials to offer the latter such as foams, hydrocolloids, hydrofibers, hydrogels, polymers, films, alginate and cotton. Spme of th research work suggests that the incorporation of kaolin in the polymeric materials will enhance their thermal, mechanical properties and drug release rate capability, cytocompatibility, hemostatic, but the absorption rate remains unaffected irrespective of the concentration of kaolin in the foams. Now a multifunctional foam composites are synthesized by incorporating kaolin in robust polyurethane and hypothesized the improved behaviour of Polyurethane for some biomedical applications. Polymeric materials of alginate, zeolite, collage, zein can be used for multifunctional wound dressing and localized clotting due to their excellent hemostatic behaviour. Since, the nano or micro particles of TiO_2 have good antibacterial properties, therefore a cost-effective, susceptible and efficient composite of Chitosan incorporated with TiO_2 particles are synthesized. In the process of wound healing or wound dressing [25, 26]

For wound healing and developing cytocompatible fibroblast for L929 cells proliferation with less apoptosis and better survival through some excellent properties such as flexibility, porosity, mechanical strength and crystallinity is requred. Banana peel contains good mineral concentration, antioxidant property, antimicrobial behaviour against fungi and bacteria therefore the synthesized nanocomposites by using powdered form of banana peel and Chitosan is more suitable for wound healing applications. Powdered banana peel acts as a reinforcing material and crosslinking agent for chitosan. The increase in banana peel powder loading may contribute to polymer-filler interaction**.** Nanocellulose has been applied in wound-dressing due to its significant water-holding ability, mechanical strength, elasticity, antimicrobial behaviour against pathogens. Nanocomposites of Polyvinyl pyrrolidone and chitosan was designed and found to be effective for wound –dressings. Both the agents are compatible and morphologically miscible with each other by forming hydrogen bonding between carbonyl groups of PVP and hydroxyl groups of nanocellulose. Scaffolds containing 3-5 wt% of nanocellulose films resist excellent blood compatibility, cytotoxicity, antibacterial property and at 5 wt% the improvement in swelling behaviour was noticed. Electrospinning method for scaffold preparation could generate high homogeneity in addition to oxygen permeation, disinfectant property for wound and dehydrating agents [27, 28].

CONCLUSION

The biomedical applications of polymeric materials are very effective and significant due to their cost effectiveness, durability, biocompatibility, biodegradability, ease of fabrication process etc. This review focused on the various latest technologies for producing functional polymer composites by adding suitable filler materials in the polymer matrix that makes theses materials potentially better for medical applications. Electrospinning, latex technology, melt-extrusion and *in-situ* method are some commonly used techniques for processing, polymer matrix composites. The mechanism of drug delivery and bioseparation inside the body parts of these functional materials is reliable as well as efficient. There are innumerable applications of polymers in the medical field such as tissue engineering, wound healing, cosmetic implants, dental implants, vascular grafts, tissue adhesives, contact and intraocular lenses, etc. But for commercialization modifications are required in polymeric materials to make theses suitable for the new treatment techniques for patients in the future.

REFERENCES

1. Ashish, C., & Balbir, K. (2012). Sorrel fiber as reinforcement in bio-composite. Journal of Environmental Science and Technology 5(5) : 343-353
2. Avella, M., Bonadies, E., Martuscelli, E., & Rimedio, R. (2001). European current standardization for plastic packaging recoverable through composting and biodegradation. *Polymer testing* 20(5) : 517-521
3. Van de Velde, K., & Kiekens, P. (2002). Biopolymers: overview of several properties and consequences on their applications. *Polymer testing* 21(4) : 433-442
4. Lucas, N., Bienaime, C., Belloy, C., Queneudec, M., Silvestre, F., & Nava-Saucedo, J. E. (2008). Polymer biodegradation: Mechanisms and estimation techniques–A review. *Chemosphere* 73(4) : 429-442
5. Carmali, S., & Brocchini, S. (2014). Polyacetals. *Natural and Synthetic Biomedical Polymers* : 219-233
6. Liu, H., Slamovich, E. B., & Webster, T. J. (2006). Less harmful acidic degradation of poly (lactic-co-glycolic acid) bone tissue engineering scaffolds through titania nanoparticle addition. *International journal of nanomedicine* 1(4) : 541.
7. Chivrac, F., Pollet, E., & Averous, L. (2009). Progress in nano-biocomposites based on polysaccharides and nanoclays. *Materials Science and Engineering: R: Reports* 67(1) : 1-17.
8. Mishra, R. K., Sabu, A., & Tiwari, S. K. (2018). Materials chemistry and the futurist eco-friendly applications of nanocellulose: Status and prospect. *Journal of Saudi Chemical Society* 22(8) : 949-978.
9. Saikia, C., Gogoi, P., & Maji, T. K. (2015). Chitosan: A promising biopolymer in drug delivery applications. *J. Mol. Genet. Med. S* 4(006) : 899-910.
10. Elnaggar, Y. S., Etman, S. M., Abdelmonsif, D. A., & Abdallah, O. Y. (2015). Intranasal piperine-loaded chitosan nanoparticles as brain-targeted therapy in Alzheimer's disease: optimization, biological efficacy, and potential toxicity. *Journal of pharmaceutical sciences* 104(10) : 3544-3556.
11. LaNasa, J. A., Torres, V. M., & Hickey, R. J. (2020). In situ polymerization and polymer grafting to stabilize polymer-functionalized nanoparticles in polymer matrices. *Journal of Applied Physics*, 127(13) {134701-27.
12. Zagho, M., Hussein, E., & Elzatahry, A. (2018). Recent Overviews in Functional Polymer Composites for Biomedical Applications. *Polymers*, 10(7):739-759.
13. . Ramakrishna, S., Mayer, J., Wintermantel, E., & Leong, K. W. (2001). Biomedical applications of

polymer-composite materials: a review. *Composites science and technology* 61(9) : 1189-1224.

14. Zafar, M., Najeeb, S., Khurshid, Z., Vazirzadeh, M., Zohaib, S., Najeeb, B., & Sefat, F. (2016). Potential of electrospun nanofibers for biomedical and dental applications. *Materials* 9(2) : 73.
15. Qasim, S. B., Zafar, M. S., Najeeb, S., Khurshid, Z., Shah, A. H., Husain, S., & Rehman, I. U. (2018). Electrospinning of chitosan-based solutions for tissue engineering and regenerative medicine. *International journal of molecular sciences* 19(2) : 407.
16. Brigger, I., Dubernet, C., & Couvreur, P. (2012). Nanoparticles in cancer therapy and diagnosis. *Advanced drug delivery reviews* 64 : 24-36.
17. Jung, K-C, Han, Min-G, Mehboob, A., Chang, S-H (2017). Performance Evaluation of Bone Plates Consisted of BGF/PLA Composite Material according to Body Fluid Exposure Conditions, *Composites Research* 30(1):21-25
18. Al-Enizi, A. M., Zagho, M. M., & Elzatahry, A. A. (2018). Polymer-based electrospun nanofibers for biomedical applications. *Nanomaterials* 8(4) : 259.
19. Liechty WB, Kryscio DR, Slaughter BV, Peppas NA (2010) Polymers for drug delivery systems. *Annu Rev Chem Biomol Eng* 1: 149-173.
20. Zagho, M. M., Hussein, E. A., & Elzatahry, A. A. (2018). Recent overviews in functional polymer composites for biomedical applications. *Polymers* 10(7) : 739.
21. Li, Z., Ramay, H. R., Hauch, K. D., Xiao, D., & Zhang, M. (2005). Chitosan–alginate hybrid scaffolds for bone tissue engineering. *Biomaterials* 26(18) : 3919-3928.
22. Lu, H. H., Kofron, M. D., El-Amin, S. F., Attawia, M. A., & Laurencin, C. T. (2003). In vitro bone formation using muscle-derived cells: a new paradigm for bone tissue engineering using polymer–bone morphogenetic protein matrices. *Biochemical and biophysical research communications* 305(4) : 882-889.
23. Mir, M., Ali, M. N., Barakullah, A., Gulzar, A., Arshad, M., Fatima, S., & Asad, M. (2018). Synthetic polymeric biomaterials for wound healing: a review. Progress in Biomaterials, 7(1), 1–21
24. Üstündağ Okur, N., Hökenek, N., Evren Okur, M., Ayla, Ş., Yoltaş, A., Siafaka, P. I., & Cevher, E. (2019). An alternative approach to wound healing field; new composite films from natural polymers for Mupirocin dermal delivery. *Saudi Pharmaceutical Journal*, 27(5): 738-752
25. Kamoun, E. A., Kenawy, E.-R. S., & Chen, X. (2017). A review on polymeric hydrogel membranes for wound dressing applications: PVA-based hydrogel dressings. *Journal of Advanced Research*, 8(3): 217–233.
26. Purwar, R., Rajput, P., & Srivastava, C. M. (2014). Composite wound dressing for drug release. *Fibers and Polymers*, 15(7), 1422–1428
27. Behera, S. S., Das, U., Kumar, A., Bissoyi, A., & Singh, A. K. (2017). Chitosan/TiO 2 composite membrane improves proliferation and survival of L929 fibroblast cells: Application in wound dressing and skin regeneration. *International Journal of Biological Macromolecules*, 98: 329–340.
28. Kamel, N. A., Abd El-messieh, S. L., & Saleh, N. M. (2017). Chitosan/banana peel powder nanocomposites for wound dressing application: Preparation and characterization. *Materials Science and Engineering: C*, 72: 543–550.