DEVELOPMENT AND CHARACTERIZATION OF CONDUCTING POLYMER BASED HYDROGEL FOR WOUND HEALING APPLICATION

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Abstract

Introduction- The normal and chronic wound healing is a global challenge. In recent decades, electrotherapy for treating such wounds emerged as a novel and efficient technique. One of the important components in wound healing electrotherapy is the hydrogel which is applied on the wound to uniformly distribute the electric current. In this work we report the development and wound healing efficacy testing of vitamin D entrapped polyaniline-chitosan composite hydrogel for electrotherapy.

Materials and methods- The vitamin D entrapped polyaniline-chitosan composite hydrogel was developed and characterized using morphological and physicochemical techniques like SEM, DSC, XRD, FT-IR, pH, conductance, viscosity, and porosity analysis. The biodegradation was studied using lysozyme and water uptake ability was studied using phosphate buffer. Vitamin D entrapment and release study was performed using ethanoic phosphate buffer. Cell adhesion, proliferation and effect of electrical stimulation was carried out by seeding dental pulp stem cells into the scaffolds and using MTT assay; the SEM images were taken to confirm the proliferation results. The wound healing efficacy of electrotherapy and developed hydrogel was studied on excision wound healing model in rats and scar free wound healing was further confirmed by histopathology analysis.

Results- The developed hydrogel was optimized for composition as 1% w/v polyaniline and 2% w/v of chitosan composite. This hydrogel showed 1455 μA conduction, 98.97% entrapment efficiency and 99.12% release of vitamin D in 48 hrs. Optimized hydrogel formulation showed neutral pH of 6.96 and had 2198 CP viscosity at 26 °C. Hydrogel showed 652.4 % swelling index and 100 % degradation in 4 weeks. The in-vitro cell culture studies performed on hydrogel scaffolds using dental pulp stem cells (DPSC) and electric stimulation strongly suggested that electrical stimulation enhances the cell proliferation in 3D scaffold environment. The in-vitro results were also supported by in-vivo excision wound healing studies suggesting electrical stimulation of the wound in the presence of the conducting hydrogel and growth factors like vitamin D heals the wound much faster (within 12 days) compared to non-treated control wounds (required 21 days for complete healing).

Discussion- The results strongly suggest that the developed polyaniline-chitosan composite conducting hydrogel acts effectively as an electric current carrier to distribute the current uniformly
through the wound surface. It also acted as drug delivery vehicle to deliver vitamin D in wound. The hydrogel provided moist environment, 3D matrix for free migration of the cells and antimicrobial activity due to chitosan supporting the faster wound healing mechanism of the electrotherapy which was confirmed through in-vitro and in-vivo experiments.

**Keywords-** Polyaniline, chitosan, composite hydrogel, wound healing, electrical stimulation, vitamin D.

**Introduction**

As per world health organization [WHO], injuries are growing and common public health issue. It is one of the main cause for deaths, when monitored across the globe annually. According to survey made by WHO, globally about 5.7 million deaths are accounted, which are 9% of total global annual deaths due to injuries and deaths represents very small portion of the injured patients. There are millions of people suffering from injuries that requires hospitalization, emergency treatments, and consultation of general practitioner or home remedies [1]. An injury is a result of wound, which refers to disruption of dermis layer and cellular continuity due to external impact on skin. Generally, there are five types of wounds: abrasion, puncture, burn, avulsion and laceration. The normal wound healing is slow and it takes minimum 21 days to complete 4 phases of wound healing including hemostasis, inflammatory/defensive phase, proliferative phase and maturation/remodeling phase [2]. Chitosan is N-de-acetylated derivative of chitin. It is most abundant biopolymer found in exoskeleton of crustacean, mollusks and insects [3]. Chitosan exhibits high mechanical strength, good film forming properties, adequate adhesion, it is non-irritant, biodegradable and biocompatible [4,5]. Chitosan based hydrogel can be made by using various crosslinking agents like genipin, glutaraldehyde and sodium tri-polyphosphate [6]. Hydrogels are three-dimensional swollen structures that contains more than 90% of water. When placed in an aqueous medium, they are able to swell and retain volume of the absorbed aqueous medium in their three-dimensional swollen network [7]. Conducting polymer hydrogels are gels containing a conducting polymer along with a supporting polymer as components, and they are swollen with water or electrolyte solution. Polyaniline, poly-pyrrole or poly(3,4- ethylene-dioxy-thiophene) are the most widely used conducting polymer which represents the conducting moiety, while cross-linked water-soluble polymers the other part of hydrogel [8].

Polyaniline (PANI) is the most widely used conducting polymer that has various applications, such as in molecular sensors, protection of metals from corrosion, gas separating membranes or in rechargeable batteries [9-11]. Polyaniline showed a desired range of conductivity, it is easy to synthesize, requires low operational voltage, offers thermal and chemical stability and it is pH-responsive polymer that has different chemical forms, based on acidic/ basic treatment [12,13]. Despite of these good advantages, PANI has some drawbacks like, poor solubility in common organic solvents, poor infusibility and poor mechanical properties [14,15]. In order to overcome these limitations, various attempts were made, which include doping PANI using specific doping techniques like, using additives or forming composite of PANI with other polymer matrix [16,17]. The composite of PANI-Polymer matrix improves its solubility, mechanical properties and PANI offers the conducting properties to the PANI/Polymer composite making it stimuli responsive (pH and external electrical stimuli). Such PANI/Polymer matrix are widely employed in sustained drug delivery if polymer matrix exhibits properties of hydrogel. Its water uptake ability allows the entrapment of drugs or actives inside 3D matrix and controlled release of the same makes it an advanced candidate for biomedical applications [18].

In this study, chitosan-PANI composite hydrogel with good mechanical properties and electrical conductivity was developed [19,20]. The recent literature were reported on synthesis of blends of chitosan with PANI or its derivatives [21-23] where chitosan may also be used as a steric stabilizer for stimuli responsive PANI colloids [24]. In the present work, initially the polyaniline was synthesized by using oxidative polymerization reaction followed by formulating chitosan-PANI hydrogel with vitamin D (as growth factor) in controlled three-dimensional matrix. In this composite
hydrogels, the polyaniline was distributed uniformly throughout in chitosan network and concentration of polyaniline was optimized by considering conduction required for wound healing application. Chitosan was selected for its biodegradable, hemostatic, antimicrobial, film-forming properties and its structure. Chitosan enables the enhancement of conducting nature of PANI due to presence of hydrogen bonds between hydrogel network and PANI. To demonstrate its significance of vitamin D loaded matrix in wound healing and for ease of cell line studies, the formulated hydrogel was lyophilized to get scaffolds of chitosan-PANI. Preliminary applications of these composites in in-vivo wound healing was further demonstrated.

Materials and Methods

**Materials**- Chitosan (Cell culture tested-Low molecular weight grade 50,000- 190000, Degree of deacetylation- 90%) was procured from sigma Aldrich, United states; Ammonium persulfate and aniline purchased from Loba chemicals, India. Vitamin D was procured from Alfa Aesar, India. All other chemicals used were of analytical grade and highest purity.

**Synthesis of polyaniline:** Polyaniline was synthesized as per the method reported by, Ibrahim et al [25]. In short, 5ml of aniline was mixed with 100 ml 1M HCl. Into this mixture100 ml of 1M ammonium persulfate solution was added as polymerization initiator. The solution was kept on magnetic stirrer for 24 hours at 1200 rpm until dark green precipitate is formed. The precipitate was washed with distilled water three times to remove free aniline monomers and recrystallized using methanol. Then, the precipitate was dried for 24 hours to get fibrous powder.

**Preparation of conducting polymer-based hydrogel (conducting hydrogel):** Chitosan was slowly added to 1% acetic acid solution, under constant stirring using homogenizer. Once the chitosan is dissolved completely, Vitamin D (dissolved in 6:4 v/v water:ethanol ratio) and polyaniline was added and stirred continuously to uniformly distribute polyaniline [25]. Vitamin D was used as growth factor (drug) as its use was previously reported for improved wound healing [26]. Further, the sodium TPP solution was added dropwise, and stirred for 30 minutes to get homogenized gel. For characterization and animal study, Hydrogel was used and for cell line studies, hydrogel was lyophilized to form scaffolds.

**Experimental section**

**Physicochemical characterization:** The appearance and color of the hydrogel was determined by visual observation. The pH of optimized batch and blank hydrogel was measured by using (ELICO LI-120, India) digital pH meter.

**Conductivity:** Conductivity of blank and optimized batch of hydrogel were determined by using two probe conductivity meter (Labramm- EQ-650, India) [27].

**Viscosity:** The viscosity of conducting hydrogel and blank hydrogel was checked by using Brookfield viscometer (DV PRO-II, USA). The torque and viscosity were recorded at 26 °C with spindle no 18 fitted on small sample adapter at different RPM (10-40) and the Newtonian behavior of the hydrogels were predicted [28].

**Scanning electron microscopy (SEM):** The porosity and morphology of the lyophilized hydrogels were studied by scanning electron microscopy (SEM) [FEI Nova Nano SEM 450, India] machine. First, the samples were coated using gold sputter coater (SPI Module sputter coater, USA). The samples were then randomly scanned, and photomicrographs were taken at the acceleration voltage of 10 kv. [29].

**FTIR Spectroscopy:** The lyophilized blank and conducting hydrogel powders were characterized by the FTIR technique. FTIR spectra were recorded using a Fourier transform infrared spectrophotometer (Shimadzu scientific instruments, model no 8400s, Japan) using KBr pellets [30]. The spectra were recorded and compared from 600 – 4500 cm⁻¹.

**Differential scanning calorimetry (DSC):** The DSC study was carried out [using Mettler –Toledo DSC-I, USA] for lyophilized blank and conductive polymer hydrogels. The samples were heated from 40°C to 300°C at the rate of 10°C/min. The inert atmosphere was maintained by purging nitrogen gas throughout the experiment at the rate of 50-70 ml/min using crimped aluminum pan for accurate results [29].
**X-Ray diffraction (XRD):** The XRD study was carried out for blank hydrogel and conducting hydrogel, using Rigaku Miniflex-600 instrument from scanning range of 20-800° [30].

**Drug entrapment efficiency:** The drug (vitamin D) loaded cross-linked hydrogel (5g) was added in 50 ml of ethanolic phosphate buffer of pH – 7.4 at 26°C for 2 h, frequent sonication (at every 20 min) was done to release all the drug entrapped in cross-linked matrix. Amount of free drug (vitamin D) determined by collecting clear supernatant by UV Spectroscopy at 262 nm. The supernatant from empty hydrogel (without cross-linker) was taken as a blank [31] the drug entrapment of cross-linked and normal matrix were compared.

**Drug diffusion study:** The in-vitro diffusion studies of the prepared Hydrogel were carried out in Franz- diffusion Cell by using 25 ml ethanolic phosphate buffer pH 7.4 temperature was maintained at 37±1°C. The acceptor compartment of the cell was filled with the 25ml ethanolic phosphate buffer 7.4 and continuously stirred with small magnetic bead. The donor compartment was filled with the hydrogel (equivalent to 50 mg of vitamin D). The 100 µl sample was withdrawn at specific time intervals to assess the release of vitamin D from the hydrogel in the donor compartment. The sink condition due to sample withdrawal was maintained by replenishing the equal amount of ethanolic phosphate buffer in the receiver compartment [32].

**Water uptake ability / Swelling behavior:** Pre-weighed scaffold was immersed in swelling medium (Phosphate buffer pH-7.4) [33,34]. At various time interval scaffolds were removed using spatula and placed on filter paper to remove excess of water and immediately weighed. The procedure was repeated and continued until no weight increase was observed. The swelling percent was calculated using equation 1

\[
Q = \frac{(M_s - M_d)}{M_d} \times 100
\]

Where, \( Q = \) Swelling Ratio; \( M_s = \) Mass in swollen State; \( M_d = \) Mass in dried State

**Biodegradation study:** The degradation of scaffolds were performed in phosphate buffer saline solution (PBS, \( \text{pH} = 7.4 \)), containing 800 mg/L of lysozyme, at 37 °C in an orbital shaker at 50 rpm for four weeks. Fresh lysozyme solution was replaced every third day. The samples were analyzed, at predetermined time (1, 2, 3 and 4 weeks). The samples were removed from the medium, rinsed with distilled water and dried in the oven at 50 °C until constant mass [35]. The degradation degree (\( \Delta m \)) was determined as the weight loss percent with respect to the initial weight of the sample and calculated using equation 2.

\[
\Delta m (\%) = \frac{m_1 - m_2}{m_1} \times 100
\]

Where, \( \Delta m = \) Degree of Biodegradation; \( m_1 = \) Initial weight of scaffold; \( m_2 = \) Weight of scaffolds after predetermined rate

**Cell proliferation studies:** The effect of electric current (1mA supplied using BioRad power supply) on the cell survival and proliferation was studied using stem cells isolated from dental pulp (DPSC). The DPSC were selected for this study as these stem cells easily undergo differentiation in the influence of growth factors like vitamin D to give the multiple differentiated cells required for better angiogenesis and neurogenesis. In the wound healing process, angiogenesis and neurogenesis are the rate limiting stages. Thus, the use of DPSC can effectively address this issue in wound healing leading to faster healing. Thus, to prove that the DPSCs can significantly survive in the developed conducting hydrogel the in-vitro cell proliferation studies were performed. The cell proliferation and cell viability for the DPSCs seeded in the conducting scaffold which were treated and not treated with small (1mA) electric current were assessed using MTT assay.

In order to determine the proliferation of DPSCs, cells were sub-cultured in 20% Fetal Bovine Serum (FBS)- DMEM-F12 with 1% penicillin-streptomycin medium. When the cells were 90% confluent; \( 1 \times 10^4 \) were seeded into two 24-well culture plates separately containing blank and conducting hydrogel scaffolds (5mm height and 4mm diameter cylindrical scaffold). The plates were incubated at 37°C in a humidified CO2 incubator.

The MTT assay was performed (\( N = 6 \) samples each) every 5 day till 15 days, for scaffolds with electrical stimulation and without electrical stimulation and absorbance readings were recorded at 570 nm [36]. Population doubling times (PDT) was then calculated based on the equation 3

\[
PDT = \frac{T \log 2}{\log FCC - \log ICC}
\]
Where, ICC is the initial cell count, FCC is the final cell count and T is the incubation time (in hours).

**In-vivo wound healing study:** Excision wound healing using wistar albino rats model was carried out after CPCSEA Clearance (Approval no: DYPIPSR/IAEC/18-19/P-09). In this study, Animals were divided into 4 groups (n=6), in which Group 1 was treated as control group (not treated with anything), group 2 as a standard (treated with Cipladine), group 3 as a blank hydrogel and group 4 as a CP based hydrogel. The full thickness excision wound was created on the back of Wister Rats in all the groups. Wound healing was monitored by measuring wound area. Wound area and % Wound Contraction was calculated using equation 4.

\[
\text{% Wound Contraction} = \frac{A_0 - A_t}{A_0} \times 100
\]

Where, \(A_0\) and \(A_t\) were initial wound area and wound area after a time interval \(t\).

**Histopathology:** After 15 days of in-vivo wound healing study, patch of 1cm x 1cm of skin sample from the healed wound were excised for histopathological studies. Healed skin of rat was fixed in neutral buffered formalin and standard histopathology procedure was followed. Tissues were trimmed longitudinally and routinely processed. Tissue processing was done to dehydrate in ascending grades of alcohol, cleared in xylene and embedded in paraffin wax. Paraffin wax embedded tissue blocks were sectioned at 3 μm thickness with the Rotary Microtome. All the slides of skin were stained with Hematoxylin and Eosin (H & E) stain. The prepared slides were examined under microscope to note histopathological lesions like, angiogenesis, inflammatory cell (Neutrophilic/lymphocytic) infiltration, edema and fibroblast, necrosis and scar tissue formation. Severity of the observed lesions were recorded as Minimal (<1%), Mild (1-25%), Moderate (26-50%), Moderately Severe (51-75%), Severe (76-100%) and distribution was recorded as colored arrows [36].

**Results and discussion**

**Appearance:** The prepared formulation was visually inspected for its color, odor and appearance. The blank hydrogel appeared to be slight yellowish translucent gel (Fig. 1a) and conducting hydrogel appeared as dark green colored translucent gel (Fig 1b). The blank scaffolds were white, porous 3D matrix (Fig. 1c) and conductive scaffolds were slight greenish 3D structure (Fig. 1d).

**pH Measurement:** The pH of conducting hydrogel was found to be neutral i.e 6.94. It was compared with pH of blank hydrogel, which was found to be 6.4. This increased pH allowed direct application of formulation on wound and did not cause any redness or irritation at the wound site in *in-vivo* animal studies.

**Conductivity:** The conducting hydrogel showed better conducting behavior 1455 μA, when compared to conductivity of blank hydrogel 0.098 μA. The previously reported results for polypyrrole based conducting hydrogel of same concentration was reported as 1849 μA, which was very close to our findings [37,38].

**Viscosity:** The viscosity of the blank hydrogel and conducting hydrogel was determined by using Brookfield viscometer. It was observed that hydrogels showed the shear-thinning behavior, as the viscosity decreased with increase stress from 3198 to 2198 cp, for blank hydrogel and from 3280 to 2208, for CP based hydrogel. The similar results were reported by Mawad et al, for single component CP based hydrogel using in-situ approach [39,40].

**SEM analysis:** The SEM images of noncross-linked (blank) and cross-linked (conducting) hydrogel were showed in figure 1e and f respectively. The obtained scaffolds showed irregular pore size ranging from100-230μm, when observed at 500x. The cross-linked batch showed more porous nature compared to batch without cross-linking, this might be due to higher interaction that occurred with TPP. The similar results were also reported by Sajesh et. al [23].

**IR Spectra spectral analysis:** The IR spectra of chitosan and conducting hydrogel is shown in figure-2. The observed frequencies for blank hydrogel (Fig. 2a) OH Stretching, N-H bending, CH Stretching of CH3 and CH2 groups and bend of NH-C=O amide were observed at 3628 cm⁻¹, 3379
cm⁻¹, 3000 cm⁻¹ and 1705 cm⁻¹ respectively. The obtained values matched with previously reported results, by Kodama et al [41]. The IR spectra of conducting hydrogel (Fig. 2a) scaffold showed frequencies for C-H stretching, O-H stretching, C-O Stretching, C=O Stretching and C-N stretching at 2864 cm⁻¹, 3495 cm⁻¹, 1022 cm⁻¹, 1649 cm⁻¹, 1270 cm⁻¹ respectively. The obtained values closely matched with the previously reported results, by Oka et al [42].

**DSC thermogram analysis:** DSC spectra are shown in figure 3a. DSC spectra of blank hydrogel indicated the sharp endothermic peak at 82.24 °C, which was related to the water loss along with broad endothermic peak at 268 °C followed by broad exothermic peak at 288 °C, which is indicative of decomposition of chitosan. The obtained values matched with previously reported values by Martin et al [22]. DSC thermogram of conducting hydrogel showed peak at 90 °C, which was related to moisture loss. The sharp endothermic peak at 117.53 °C which indicated the degradation peak of vitamin D along with broad endothermic peak at 133.69 °C followed by broad exothermic peak at 144.69 °C which is indicative of decomposition of polyaniline. The endothermic peak at 270 °C followed by exothermic peak at 292 °C confirmed the degradation of chitosan, the obtained results matched closely with results previously reported by Thanpitcha et al. [43].

**XRD spectral analysis:** The diffractogram of the blank hydrogel and conducting hydrogel is shown in the figure- 3b. The characteristic broad peaks of blank hydrogel were observed at 13 and 17 degrees 2θ in crystallographic planes, suggesting amorphous natured chitosan. The obtained values matched with the previously reported Badhe et al. [44]. The conducting hydrogel comprised of a dense network structure of interpenetrating polymer chains cross-linked to each other by TPP. Thus, the diffractogram of vitamin D-loaded conducting hydrogel exhibited sharp peaks at 130 and 170 represents chitosan, 250 represents vitamin D and broad peak at 430 represents amorphous nature of PANI. The obtained results are similar to the previously reported results by Sultana et al [45].

**Drug entrapment efficiency / Drug diffusion study:** The entrapment efficiency for conducting hydrogel was found to be 98.97%. The reported standard drug entrapment efficiency for chitosan scaffolds was 97-100%. The in-vitro release profile of vitamin D was found to be 99.12 % through the franz diffusion cell using dialysis membrane in 48 hours, of vit D (Fig. 4a). The reported results for poly-pyrrole based hydrogel showed the release of Vitamin D is 99% after 52 hours. It can be predicted that cross-linking will increase release time [46].

**Water uptake ability / Swelling behavior:** The medium water uptake ability i.e. 652.4% was assessed by determining the swelling index of scaffolds in phosphate buffer at 37 °c. Results showed in figure 4b that, after 70 minutes there was no significant increase in the water uptake ability of scaffolds. The previous reports by Mawad et al. suggested 787.69% water uptake ability for poly-pyrrole based scaffolds, which matches closely with previously reported results [40].

**Biodegradation study:** The study was continued till scaffolds disappeared completely. From the obtained results (Fig. 4c), it was observed that scaffolds showed gradual weight loss till 4th week and was completely degraded till the end of 4th week. Some previous reports showed 91-94% of biodegradation after 7th week. Conducting hydrogel scaffold degraded within 4 week, which might be attributed to molecular weight of chitosan [45].

**Cell proliferation study:** The cell proliferation study was carried out by using (Dental Pulp Stem Cells) DPSC cells isolated from dental pulp. During these studies, the scaffolds were subjected to electrical stimulation for 15 days, (Fig. 5a). It was observed that, the electrical stimulation helps in faster proliferation of cells compared to non-electrical stimulated scaffolds (Fig. 5b). Some previously reported papers showed the proliferation of stem cells over 21 days when seeded in scaffolds [significance ** p≤0.01 and *** p≤0.005] [47,48]. The SEM images supporting the improved proliferation with electrical stimulation were shown in figure 5c, it was concluded that, electric current supports the cell proliferation.

**In-vivo wound healing study:** The results of wound healing animal studies, using electrical stimulation (Fig. 6b) are shown in figure 6. The % wound contraction results were statistically analyzed by one-way ANOVA (n=6), ***p<0.01, *p<0.05. Wound healing in the animals treated with conducting hydrogel was found to be significantly faster compared to control and blank hydrogels (Fig. 6a). Thus, the study supports the observations that electrical stimulation of the
wound with conducting hydrogel helps in faster wound healing (within 12 days) compared to control (which took 21 days to heal completely) [49].

**Histopathology:** Microscopic examination of skin showed mild epidermal hyperplasia with fibrosis in animals belonging to control however, other groups showed normal epidermis and dermis. The obtained results are shown in figure 6c. It can be clearly observed that Group III (blank hydrogel) and Group IV (conducting hydrogel) showed collagen synthesis, fibroblast migration and epithelization suggesting healthy and flexible skin tissue generation without scar tissue. Whereas, Group II (Marketed formulation) only showed epithelization, fibroblast migration and necrosis which indicated scar tissue formation. Thus, it can be claimed that both blank and conducting hydrogels helped in scar free wound healing and electrical stimulation of conducting hydrogel helped in faster wound healing without scar tissue formation. The same can be observed in the healed skin images of the animals in figure 6c.

**Discussion –**

Injuries and wound are some of the most common health concern in our day-to-day life. Generally, small injuries like abrasion or cuts heal naturally without any infection and with little care. If the wounds are big, like laceration, avulsion, incision or amputation, emergency medical help is required. Many of these wounds heal at slower rate due to infections and patient health/age conditions. There is a separate class of injuries called non-responding or chronic injuries which is mainly observed in burn, diabetic and obese patients. These types of injuries pose a potential burden on our healthcare system and patients’ financial condition too. There are variety of treatments available for these kind of wounds including hyperbaric oxygen therapy, plastic surgeries, grafts, negative pressure therapy and electrotherapy. All these techniques have their advantages and disadvantages but electrotherapy proved to be more useful and economical option in all. Electrotherapy treatment apply small electric current (200 – 800 µA) which mimics the current of injury and helps the wound faster. However, to get the maximum benefit of the therapy an equally effective hydrogel is required which can distribute the applied electric current throughout the wound. This research work focused on developing optimized conducting hydrogel, which is capable of uniformly distributing the electric current throughout the wound. In addition to the distribution of electric current, in this work, the developed hydrogel also act as a drug delivery vehicle delivering vitamin D as growth factor. In addition, the polyaniline-chitosan hydrogel base also act as antimicrobial wound closure to protect the wound from secondary infection. The highly biocompatible and biodegradable nature of the hydrogel provides the moist 3D environment to the wound and allows the cells (fibroblast, keratinocyte) to migrate in 3D environment to heal the wound faster. The daily electrical stimulation enhances the migration of the cells and moist environment with vitamin D (supporting angio and neuro genesis) helps the wound to heal with normal healthy skin without scar tissue.

Though the study reported here showed very promising results with the developed hydrogel, there are some limitations. The study was performed using 1mA current, which is slightly higher from the actual current of injury; the optimization of the current will provide better results. The biodegradation of the hydrogel was established in this study but the non-degradable polyaniline (though in small amounts) needs to be addressed. By understanding these limitations, the further modification of the hydrogel with novel biodegradable and effective conducting materials are planned. Further studies with new drug entity immobilization in hydrogel for the same application is also planned.

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References


Figures
Figure 1: Appearance and morphology of the gel and scaffolds: a and b – Blank and conducting hydrogel respectively; c and d – Blank and conducting hydrogel scaffolds respectively; e and f – SEM images of blank and conducting hydrogel scaffolds respectively.

Figure 2: IR spectra of blank hydrogel and conducting hydrogel

Figure 3: a – DSC spectra blank and conducting hydrogel; b – XRD spectra of blank and conducting hydrogel.
Figure 4: a - Drug release (of vitamin D); b - Water uptake; and c – Degradation studies of conducting hydrogel
Figure 5: a - Electrical stimulation to scaffolds; b - Graph of Cell proliferation studies performed using MTT assay [** p≤0.01 and *** p≤0.005]; c - SEM images of cells seeded scaffolds with and without electrical stimulation.

Figure 6: a - % wound contraction graph [** p≤0.01 and * p≤0.05]; b – application of conducting hydrogel and electrical current at different time intervals (every 3 days); c - Histopathology results [Black arrows indicates scar tissue formation, Red arrows indicates healing wound/initiation of re-epithelization, Blue arrows indicates edema and fibroblasts and Yellow arrow indicates necrosis, Green arrows in group III and group IV indicated initiation of collagen regrowth at wound site].
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