ABSTRACT

Mr. Atif Islam
PhD scholar, DMME, PIEAS

The aim of this work is to develop novel pH sensitive blends having hydrogel properties using biocompatible polymers. Blends of chitosan (CS) and poly (vinyl alcohol) (PVA) are prepared and a novel approach is used to crosslinked these blends with tetraethoxysilane (TEOS) to give network structure and hydrogel properties. These CS/PVA blends are fabricated into different forms such as hydrogel films, nanofibers mat and scaffolds. Fourier transform infrared (FTIR) analysis confirmed the presence of the incorporated components keeping their structure and formation of the siloxane linkage between CS and PVA in hydrogel blends, nanofibers and the scaffolds. The developed blends in different media such as water, pH and ionic media showed different responses in swelling and changed by varying the amount of crosslinker and PVA in CS/PVA blends. The swelling in water is decreased with increasing crosslinker amount and PVA content. The speed of water uptake is affected by increasing crosslinking density which initially exhibited linear increase and reached to a maximum value around half an hour. Crosslinking percent and thermal stability are increased with increasing the amount of crosslinker. The swelling response of the blends against pH showed low swelling in acidic and basic pH while maximum swelling is exhibited at neutral pH. This unique behavior along with biocompatibility of the components made them suitable for oral delivery of drugs and has been exploited as enteric coating for commercial aspirin tablets. The dissolution test of enteric coated aspirin tablet in simulated gastric fluid (SGF, pH 1.2) showed 7.11% of aspirin release over a period of 2 h, whereas, a sustained release of remaining aspirin (83.25 %) is observed in simulated intestinal fluid (SIF, pH 6.8). The hydrogel blends are also used for loading of progesterone and dexamethasone. The released profile of progesterone (PG) loaded hydrogels showed 10.1% release for 2 h in SGF and a consistent release of remaining drug (81.3 %) up to 6 h in SIF. The released profile of dexamethasone loaded blends showed 9.4% of drug release over a period of 2 h in SGF and showed a consistent release of remaining drug up to 7 h in SIF.

The influence of TEOS on viscoelastic and structure properties of hydrogel blends is studied. The viscoelastic properties showed that both the storage modulus $G'$ and loss modulus $G''$ decreases as the temperature increased. The increased value of storage modulus at room
temperature with increasing frequency indicates the stable structure of the gel. DSC results exhibited the presence of free, intermediate and bound water in the hydrogels. The biomechanical properties of hydrogel blends and scaffolds exhibited that the tensile strength (TS) is increased with increasing crosslinker percent while elongation at break is decreased. Whereas, the TS is decreased with increase in PVA amount and elongation at break is increased. The surface properties showed the hydrophilic behavior of the hydrogels and scaffolds. The contact angle is increased with increase in the amount of crosslinker, PVA and irradiation dose. The structural analysis by XRD showed the characteristics peaks belong to chitosan and PVA. It also showed an increase in the crystallinity of blends, nanofibers and scaffolds on increasing the PVA content which is attributed to the improved interaction between crosslinker, CS and PVA. Scanning electron micrographs of blends showed porous network structure which is responsible for their swelling. The micrographs of nanofibers exhibited the average size of the nanofibers is in the range of 40 to 100 nm.

The conductivity studies of CS/PVA films are also carried out using impedance spectroscopy. The conductivity of the CS/PVA blends is increased from $2.93 \times 10^{-12} \text{ } \Omega^{-1}\text{cm}^{-1}$ to $10.1 \times 10^{-12} \text{ } \Omega^{-1}\text{cm}^{-1}$ as crosslinking is increased from 2 to 6 %. Further increase in the amount of crosslinker reduced the conductivity and minimum value of $0.96 \times 10^{-12} \text{ } \Omega^{-1}\text{cm}^{-1}$ is observed in 10 % crosslinked blend. The conductivity also increased with increasing temperature up to 403K showing the increase in the number of effective charge carriers at higher temperature in the blend.

The cytotoxicity of the hydrogel blends and scaffolds is investigated with standard methods using human fibroblast cells (F121, F192 and F84) for indirect method and human dermal fibroblast cell (F121) for direct method. The data revealed that these materials are nontoxic, viable to the cells and helpful in the growth of the cells, can be used for drug delivery, tissue engineering and other biomedical applications. The cell viability of the nanofibers is investigated by direct method using human cancerous bone cells (MG63). The obtained results showed that cancerous bone cells did not proliferate in the presence of these nanofibers. To conclude, the properties and the controlled drug delivery behaviour of the developed material are quite promising. Furthermore, it has the flexibility to be changed into different forms such as: hydrogel, films, nanofibers and scaffolds.