ABSTRACT

The lack of treatment options for traumatic brain injury has inspired great interest in the neural tissue engineering arena, which is streamlined by the use of polymeric-engineered nerve guidance conduits. The complex and intricate nature of the neural regeneration process has posed as an immense challenge in tissue engineering, despite recent advances in the field. Herein, an innovative mechanistic forecast to augment the regeneration of transected nerves, independently of drug therapy is described, through the use of two dimensional polycaprolactone/cellulose acetate phthalate thin polymeric films and nanofibrous platforms. These scaffolds were modified to impart favourable morphological, chemical, and biological cues to facilitate enhanced neural cell attachment and proliferation by firstly chemically modifying the films utilizing sodium hydroxide, potassium hydroxide and ethylenediamine to impart hydroxyl and amine moieties onto the surface of the films. Thereafter, biomolecules were immobilized on the film surface via genipin crosslinking. Various characterization analyses were undertaken to prove the suitability of the modified scaffolds for neural tissue engineering, such as FT-IR, DSC, XRD, TGA, SEM, porosimetric and surface area analyses, mechanical integrity testing, hydrophilicity analyses, biomolecule quantification, *In Vitro* degradation and water-uptake, *In Vitro* cytotoxicity and finally, cell attachment quantification. The hydrolysis and aminolysis treatments successfully reduced the water contact angle of the films from 71.60 to 50.64, 55.37 and 67.68°, respectively. An enhanced surface roughness is advantageous for neural tissue engineering scaffolds and was enhanced upon chemical functionalization from 35.43 to 53.03, 74.73 and 55.17, respectively. The mechanical tensile strength of the chemical functionalized films was reduced from 8.01 MPa to 6.78, 7.87 and 5.43 MPa, respectively. However, these values still fell within the range of acceptable tensile strengths for nerve tissue engineering. The BET surface area was increased from -0.40 to 6.49, 1.47 and 4.05 m^2/g. The BET cumulative volume of pores was also increased upon chemical functionalization. *In Vitro* cell attachment was quantified using a trypan blue exclusion assay and the results indicated that chemical functionalization enhanced cell attachment from 29.30 to 36.62, 41.58 and 55.44%, respectively. Biomolecules were immobilized on the aminolyzed films which resulted in an increase in all of the parameters discussed above: the water contact angles were reduced to <40°, the tensile strength was enhanced to >10 MPa, the BET surface area was increased to 33.14 m^2/g and the cell attachment was significantly improved to 123.72%. A BCA protein assay proved the presence of each biomolecule on the films. The fabrication of the biomolecule modified nanofibrous platforms resulted in an even further improvement of scaffold properties due to the extracellular matrix-mimicking nature of nanofibers. The surface roughness of the nanofibrous platforms was improved to 448.33 m^2/g. A BCA protein assay quantified the concentration of attached biomolecule on the nanofibrous platform, proving successful biomolecule immobilization. The BET surface area was improved to 16.33 m^2/g. The BET cumulative volume of pores was improved to 125.45 m^2/g, with an interconnected pore system with parallel slit-like pores which can facilitate the permeability of the nanofibrous platform to aid the efflux of wastes and influx of nutrients for attached cells. This investigation ultimately highlighted the success of the enhancement of neurocompatibility of the films and nanofibers using chemical functionalization as well as biomolecule immobilization.