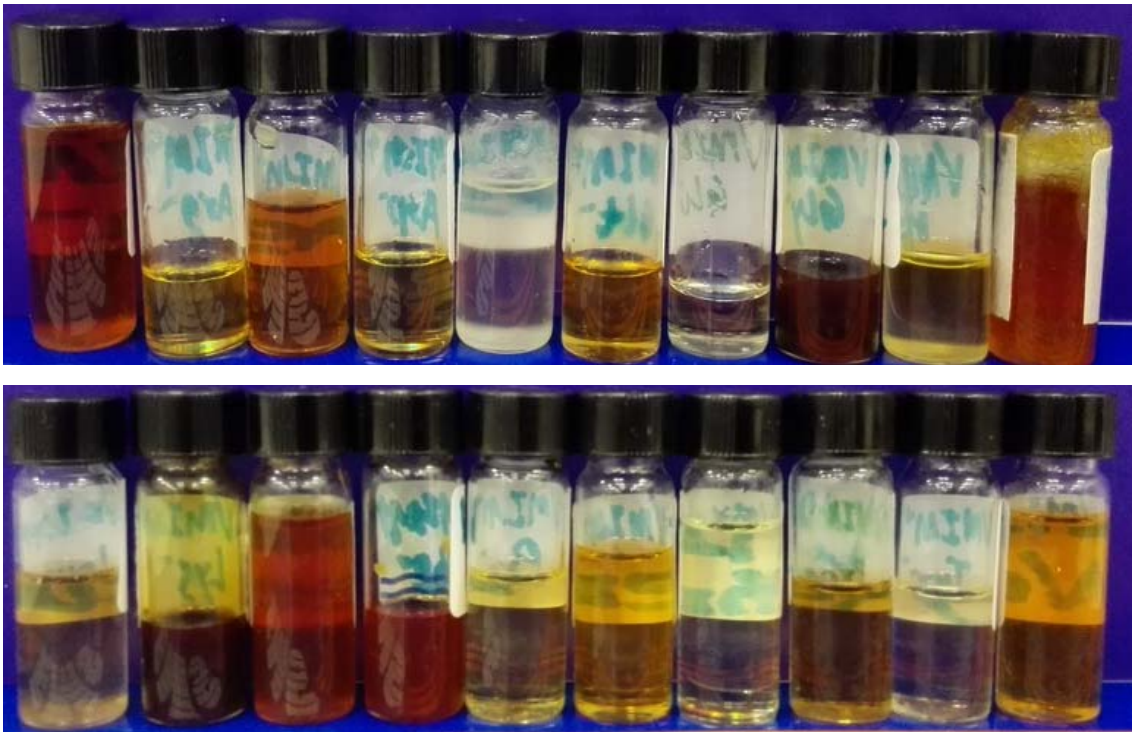
Approximately 40% of lipophilic therapeutic molecules are rejected because of their poor aqueous solubility and formulation-stability issues, which demand the development of novel carrier vehicles for hydrophobic drugs. Currently employed techniques such as emulsions, liposomes, micelles and nanoparticles suffer from disadvantages of the fast and non-specifc clearance from circulation by reticulo-endothelial system (RES) cells, their metastable nature, limited drug loading capacity, need to co-formulate with surfactants and co-solvents, low drug loading efficiency, and issues of drug precipitation and crystallization.

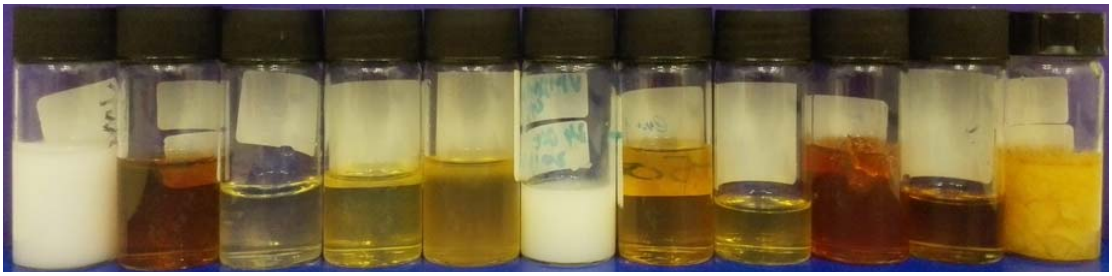
The development of polyelectrolytes-based nanogels with affinity for both water and organic liquids was proposed for the delivery of hydrophobic drugs, to overcome the shortcomings of currently employed carrier vehicles. In this work, 20 polymerizable room temperature ionic liquids with the cation being 1-vinyl-3-methylimidazolium (VMIM) and the anions being 20 natural amino acids were synthesized; the synthesis of their co-polymeric gels with 1-vinyl-2-pyrrolidone (NVP) and 2-hydroxyethyl methacrylate (HEMA), as well as the swelling capacity of the resulted gels in water and a series of organic solvents were investigated. The results showed that NVP cannot co-polymerize with the 20 polymerizable ionic liquids to give gels by aqueous solution co-polymerization, while HEMA can co-polymerize with 16 in the 20 polymerizable ionic liquids to give gels. All 16 gels showed swelling capacity in water, DMSO and DMF, while some gels also showed swelling capacity in THF, NMP and ethanol. By using Ibuprofen as a model drug and poly(HEMA-co-VMIM-Arg) as the model gels, the uploading and *in vitro* release of the hydrophobic drug onto the gels were investigated, and the results showed much better Ibuprofen uploading capacity using ethanol as the solvent compared with using water as the solvent. Nanoparticulate poly(HEMA-co-VMIM-Arg) gels were synthesized with nanoemulsion co-polymerization method and sonicating precipitation method respectively, their particle size/zeta potential were characterized, and the biocompatibility was also assessed with MTT assay using L929 mouse cell line. The results showed that a typical particle size of the nanoparticulate poly(HEMA-co-VMIM-Arg) gels prepared by the sonicating precipitation method was 186.9 nm, the PDI was 0.364 and the typical zeta potential was -20.4 mv, while particle size of the nanoparticulate poly(HEMA-co-VMIM-Arg) gels prepared by the nanoemulsion method was polydispersed and the data quality was too

poor. The nanoparticulate poly(HEMA-co-VMIM-Arg) gels showed little cytotoxicity to L929 mouse cells according to the MTT Assay.

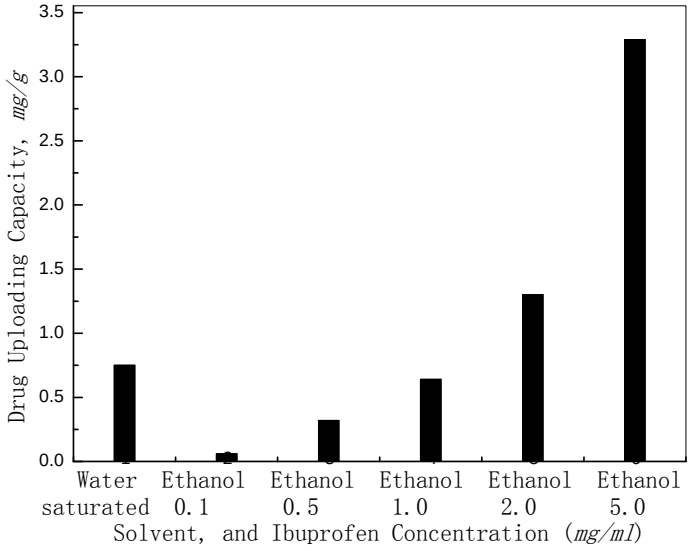
In conclusion, the co-polymeric nanogels based on polymerizable ionic liquids with affinity for both water and organic solvents are promising carrier vehicles for hydrophobic drugs, while it was also recommended that the polymerizable ionic liquids of VMIM and amino acids are not the best for the preparation of such carrier vehicle in the term of the swelling capacity in water as well as in organic solvents.



Polymerizable ionic liquids with the cation being 1-vinyl-3-methylimidazolium and the anions being twenty natural amino acids. From left to right, upper row: Ala, Arg, Asn, Asp, Cys, Glu, Gln, Gly, His, Ile; lower row: Leu, Lys, Met, Phe, Pro, Ser, Thr, Tro, Tyr, Val



Co-polymeric gels of HEMA with the 16 ionic liquids, as well as PolyHEMA gels, and the reaction solutions of the 4 ionic liquids with HEMA. From left to right, upper row: PolyHEMA, Ala, Arg, Asn, Asp, Cys (no gels), Glu, Gln, Gly, His, Ile; lower row: PolyHEMA, Leu, Lys, Met (no gels), Phe, Pro (no gels), Ser, Thr, Tro, Tyr (no gels), Val



Effect of solvent and concentration on Ibuprofen uploading