ABSTRACT

BACKGROUND: Although, TNBC is known for the absence of specific receptors such as ER, PR and HER2, there are still other expressions such as EGFR, c-KIT and CK-5/6 which can be targeted for treatment of TNBC.

OBJECTIVES: The aim of this work is to develop an efficient drug delivery system that can reach the tumour site effectively to treat TNBC.

METHODOLOGY: The immunonanoscaffold was prepared by nanoprecipitation followed by MBS conjugation. Physicochemical characterisation was performed by TEM, particle size, polydispersity index, zeta potential, entrapment efficiency and drug release. Antibody conjugation efficiency was assessed by SDS-PAGE and BSA protein assay. Stability of the INS in normal saline was also studied. *In vitro* cytotoxicity, cellular uptake and cell cycle analysis was performed using the cell line. The impact of treatment on the gene expression was performed by RT-PCR. The athymic mice was used to study in-vivo anti-tumour activity and targeting efficiency of INS.

RESULTS: All formulations show excellent drug loading and sustained drug release over 48 hours. The SDS-PAGE and BSA protein assay results confirm the conjugation of c-KIT, CK-5/6 and EGFR antibodies in the respective INS formulation. The formulations also found stable for 30 days. EGFR INS show significantly higher efficiency ($p<0.05$) then the other two INSs in all tests. The three INS formulations show excellent tumour reduction, better performance in pharmacokinetics study and *in vivo* imaging study, with more concentration and negligible elimination in comparison with plain drug and nanoscaffolds. Moreover, the image taken 24 hours post administration in athymic nude mice show INS formulation accumulation in tumour site.

CONCLUSION: The study underlines the opportunity of antibody anchored nanoscaffold mediated drug delivery for TNBC treatment.