

## ABSTRACT

This work aims towards addressing various challenges encountered in cancer therapy viz. non targeted delivery of drugs, development of multi-drug resistance by the cancer cells, toxicity caused by the carriers and poor bioavailability of certain potent drugs. This was done by the synthesis and characterization of stimuli responsive nanocarriers (nanoparticles, nanoconjugates and nanoassemblies) for targeted delivery of a multiple chemotherapeutic drugs specifically towards cancer cells. They were also adorned with additional features for exploring various facets of cancer treatment like magnetic hyperthermia, photothermal therapy and angiogenesis.

The work was executed in the following steps:

- 1. Designing surface functionalized multifunctional nanoconjugates**
- 2. Development of amphiphilic polymeric nanoassemblies**
- 3. Developing self-therapeutic nanocarriers by pro-drug strategy**

All the three classes of nanocarriers were synthesized by various strategies, duly characterized and analyzed for their targeted anticancer loading and drug release potential.

The synthesized multifunctional nanoconjugates were characterized as follows.

<b>Properties</b>	<b>Technique/Instrument</b>
Structural Elucidation	IR Spectroscopy, EDAX
Morphology and Size	SEM, HRTEM, DLS
Optical	UV-Vis & Fluorescence Spectroscopy
LCST of thermoresponsive polymer	Variable Temperature DLS
Thermal	TGA
Magnetic	VSM, Magnetic Hyperthermia experiments
Photothermal	Measurement of heating capacity post NIR laser irradiation
Antiangiogenic Potential	Ex-ovo CAM Assay
Drug Loading and Release	UV-vis Spectroscopy

The synthesized nanoassemblies were characterized as follows.

<b>Properties</b>	<b>Technique/Instrument</b>
Structural Elucidation	NMR & FTIR Spectroscopy, GPC
Morphology and Size	FESEM, HRTEM, DLS, AFM
Self-assembly	<b>Vesicles:</b> FTIR, self-quenching, fluorescence spectroscopy & microscopy <b>Micelles:</b> CMC determination by pyrene encapsulation
Drug Loading and Release	UV-vis Spectroscopy

The nanocarriers were assessed for the ability to encapsulate hydrophilic as well as hydrophobic drugs. Doxorubicin hydrochloride and curcumin were selected as the model drugs. The release profiles were assessed by subjecting the carriers to various physiological stimuli viz. pH, temperature, light and enzymes. The combination indices to determine the synergistic action of various facets employed for cancer therapy were calculated. A selective tumor homing was observed that presents the potential of the carriers in causing multi-drug resistance (MDR) reversal. The morphology of the nanocarriers was also found to have an effect on this phenomenon. All the nanocarriers were analyzed for their anticancer drug release potential by preclinical evaluations as well. In-vitro studies were performed on cancer as well as non-cancer cell lines. The antiangiogenic potential was demonstrated ex-ovo on chick embryo. The in-vivo studies were performed by induction of hepatocellular carcinoma on nude mice model. The efficacy of drug delivery systems for tumor regression and suppressing the cardiotoxicity of DOX was demonstrated by qualitative as well as quantitative examinations.