## TABLE OF FIGURES

<table>
<thead>
<tr>
<th>FIGURE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Breast cancer incidence in India by the International Agency for Research on Cancer (WHO)</td>
</tr>
<tr>
<td>1.2</td>
<td>Molecular classification of breast cancer</td>
</tr>
<tr>
<td>1.3</td>
<td>Taxol, the commercial formulation and chemical structure of Paclitaxel</td>
</tr>
<tr>
<td>1.4</td>
<td>ROS generated in cells lead to the activation of NF-κB and its downstream</td>
</tr>
<tr>
<td>1.5</td>
<td>Nuclear factor kB (NF-κB) activation affects all six hallmarks of cancer through the transcription of genes involved in cell proliferation, angiogenesis, metastasis, inflammation and suppression of apoptosis as identified in both cell lines and tissue samples</td>
</tr>
<tr>
<td>1.6</td>
<td>NF-κB may regulate self-renewing breast cancer stem cells and induce production of extracellular proteins for generating cancer stem cell niche</td>
</tr>
<tr>
<td>1.7</td>
<td>A variety of drugs that inhibit NF-κB have been classified according to their molecular targets</td>
</tr>
<tr>
<td>1.8</td>
<td>Effect of EGCG on EGFR, MAPK cascades, and activation of the transcription factors AP-1 and NF-κB</td>
</tr>
<tr>
<td>1.9</td>
<td>Chemical structures of the major tea polyphenols</td>
</tr>
<tr>
<td>1.10</td>
<td>Mechanisms of action of EGCG</td>
</tr>
<tr>
<td>1.11</td>
<td>Factors influencing EGCG bioavailability: Factors enhancing plasma levels of EGCG are listed to the left, those that diminish bioavailability can be found on the right</td>
</tr>
<tr>
<td>1.12</td>
<td>Passive and active targeting approaches of nanoprobes in cancer diagnosis.</td>
</tr>
<tr>
<td>1.13</td>
<td>Types of nanocarriers for drug delivery.</td>
</tr>
<tr>
<td>2.1</td>
<td>Chemical structures of PLGA, PVA, Paclitaxel and EGCG</td>
</tr>
<tr>
<td>2.2</td>
<td>Characterization of dual drug-loaded nanoparticles. SEM images of PLGA-PVA nanoparticles prepared using (A) acetone and (B) Acetone: Dichloromethane (1:1) solvent mix as the oil-phase, (C) Drug release obtained for Ptx and EGCG. (D) TEM image of drug-loaded nanoparticles prepared using Casein in the aqueous phase instead of PVA</td>
</tr>
</tbody>
</table>
2.3 Schematic of the synthesis scheme (emulsion-precipitation) for preparing dual drug-loaded PLGA-Casein core/shell nanoparticles

2.4 Size and morphological characteristics of core/shell nanoparticles.

2.5 Hydrodynamic diameter measured using DLS (A) PLGA-Ptx core-190.5 ±11nm, (B) dual-drug loaded core/shell nanoparticles- 230.9 ± 31 nm and (C) void core/shell nanoparticles-168 ± 17 nm

2.6 Hydrodynamic diameter variations of the void core/shell nanoparticles in various media viz., saline, PBS and PBS containing serum at different time intervals (0, 24, 48h). (B) Zeta potential variations of the void core/shell nanoparticles in saline, PBS and PBS containing serum at 0, 6, 24 and 48 h.

2.7 Hydrodynamic diameter variations of dual drug-loaded core/shell nanoparticles in various media viz., saline, PBS and PBS containing serum at different time intervals (0, 24, 48h). (B) Zeta potential variations of the same in saline, PBS and PBS containing serum at 0, 24 and 48 h.

2.8 Qualitative evaluation of core/shell and drug-loaded core/shell nanoparticles. (A) Raman spectra of PLGA, casein and PLGA–casein core/shell nanoparticles. (B) Raman spectra of EGCG, Ptx and dual-drug-loaded core/shell nanoparticles.

2.9 FTIR spectra showing characteristic peaks of PLGA, Casein, EGCG, Ptx and dual-drug loaded PLGA-Casein nanoparticles.

2.10 In vitro release of EGCG and Ptx showing a sustained release for 10 days in PBS at 37 °C, pH 7.4

2.11 Release profiles from nEGCG (core/shell nanoparticles with only EGCG), nPtx (core/shell nanoparticles with only Ptx), cEGCG (profile of EGCG from dual-drug loaded core/shell nanoparticles), cPtx (profile of Ptx from dual-drug loaded core/shell nanoparticles), CF_nPtx (casein free PLGA core with Ptx) (B) pH variation with time recorded in the release medium containing dual-drug loaded core/shell nanoparticles.

2.12 In vitro release of EGCG and Ptx from the combination nanoparticles in 20% serum containing PBS (pH 7.4)
3.1 In vitro hemocompatibility of bare core/shell nanoparticles.

3.2 In vitro immunological and toxicological analysis of bare core/shell nanoparticles.

3.3 In vivo serum cytokine analysis of 10 mg kg\(^{-1}\) nanoparticles administered to SD rats showing cytokine induction levels comparable to that observed before particle administration. \(^*P < 0.05\) (significant)

3.4 Histopathological analyses of liver, kidney and spleen sections after i.v. administration of drug-loaded core/shell nanoparticles, showing intact tissue morphology, similar to the control tissue. Scale bars represent ~50 mm

3.5 Plot showing percentage of ICG remaining in the dye-loaded nanoparticles up to 24 h

3.6 Nanoparticle biodistribution study on SD rats. The nanoparticles were loaded with Indocyanin Green (ex/em: 760/830 nm), injected via the tail vein at a concentration of 10 mg kg\(^{-1}\) and imaged using a Kodak in vivo imaging system

3.7 In vivo pharmacokinetics of i.v. administered Ptx- and EGCG-loaded core/shell nanoparticles in SD rats by HPLC.

4.1 Schematic of antibody conjugation to core/shell nanomedicine through EDC-NHS conjugation chemistry. Inset depicts the SEM image of the targeted core/shell nanomedicine

4.2 (A) Antibody conjugation efficiency plot showing concentration of antibody used versus conjugation efficiency (%); (B) Drug release exhibited by the antibody conjugated combination nanomedicine

4.3 Particle uptake study on MDA-MB-231 cells using flowcytometry and confocal microscopy. (A) targeted combination nanomedicine (B) non-targeted combination nanomedicine

4.4 Non-targeted and targeted particle uptake at 4°C in MDA-MB-231 cells using flowcytometry
4.5 Cytotoxicity and DNA quantification assays done on MDA-MB-231 cells (48 h). Cytotoxicity of (A) EGCG (bE, nE); (B) Ptx (bP, nP); (C) DNA quantification using bare and nano Ptx and EGCG (48 h). The controls are DNA content @15h (before doubling point of MDA-BB-231 viz., 27h) and 48h (after doubling point); (D) Cytotoxicity of combination (bC, CN, TCN) (48 h). p-values: * <0.05 and ** <0.01. Doubling time (DT)

4.6 Cytotoxicity assay done on MCF7 cells. Cytotoxicity of (A) Ptx (bP, nP); (B) EGCG (bE, nE); (C) combination (bC, CN). p-values: * <0.05 and ** <0.01

4.7 Annexin V-Propidium iodide apoptosis assay performed on MDA-MB-231 cells using nP, nE, CN and TCN. p values: * <0.05, ** <0.01 and ***<0.005. Untreated control (UT)

4.8 p21 gene expression in MDA-MB-231 done after subjecting the cells to nP, nE, CN and TCN by qPCR. p-values: * <0.05 and ** <0.01

4.9 Representative images of isolated nuclei from drug sample treated MDA-MB-231 cells (A) Bright field; (B) DAPI stained nuclei at 20X magnification

4.10 (A) Immunoblotting done to evaluate the activation of NF-kB in nanomedicine MDA-MB-231 cells; (B) Densitometric analysis of the bands obtained for NF-kB; (C) qPCR analysis of MMP9, BIRC5 and VEGFA genes in MDA-MB-231 cells. p-values: * <0.05 and ** <0.01

4.11 (A) Migration assay; (B) Invasion assay and (C) Adhesion assay performed on MDA-MB-231 cells. * indicates p<0.05 and ** p<0.01. Untreated control (UT)

4.12 Response of MDA-MB-231 cells to sequential addition of EGCG and Ptx at EGCG + Ptx concentrations (A) 80μM + 10 nM and (B) 40μM + 10 nM. EGCG pre-incubation was done for 1, 3 and 6 h 15 following which Ptx was incubated for the rest of the time till 48h. p value *<0.05

4.13 (A) Flowcytometric quantification of P-gp expression in MDA-MB-231 after continued culturing in Ptx; (B) Expression of ABCB1 gene quantified
through qPCR; (C) Flowcytometric quantification of P-gp expression after nanomedicine treatment. p-values: * <0.05 and ** <0.01. Untreated (UT)

5.1 (A) Suspended organoids in culture flasks at Day-0; (B) Cell outgrowth from organoid (Days 7-13); (C) Increased cell outgrowth with time; (D) Passage-1 of cells harvested from the organoid culture

5.2 Immunohistochemistry images (A) ER expression (P4), (B) PR expression (P4), (C) HER2 expression (P8) and (D) EGFR expression (P1)

5.3 Cytotoxicity on patient samples done using Ptx, EGCG and their combination in bare, nano and targeted nano forms. (A) P1, P2, P3 are EGFR+ samples; (B) P4, P5, P6 are ER+/PR+ sample. p values * <0.05 and **<0.01

5.4 Cytotoxicity on patient samples done using Ptx, EGCG and their combination in bare, nano and targeted nano forms. (A) P7, P8 [HER2 3+] and P9 [ER+/PR+/HER2 3+] samples; (B) P10 [PR+/HER2 3+], P11 [ER+/PR+/HER2 2+] P12 [ER+/HER2 2+] sample. p values * <0.05 and **<0.01

5.5 Cytotoxicity on patient samples done using Ptx, EGCG and their combination in bare, nano and targeted nano forms. P13 and P14 [HER2 2+] samples. p values * <0.05 and **<0.01
LIST OF TABLES

Table 1.1.  List of nanoparticles developed using various biocompatible materials
Table 1.2.  Type, characteristics, functions and application of EGCG nanoparticles
Table 2.1.  Effect of drug/polymer ratios on drug encapsulation efficiency
Table 2.2.  In vitro release modelling for nanomedicine combinations
Table 3.1.  Plasma pharmacokinetic parameters of bare EGCG, Ptx and the nanocombination of the drugs after i.v administration in SD rats
Table 5.1.  Surface receptor profile of breast cancer patient samples (n=14)
Table 5.2: Combination indices derived for combination nanomedicine at 10 + 50 (nM + µM) Ptx + EGCG combination