Paclitaxel delivery by micro/nano- encapsulation using layer-by-layer assembly

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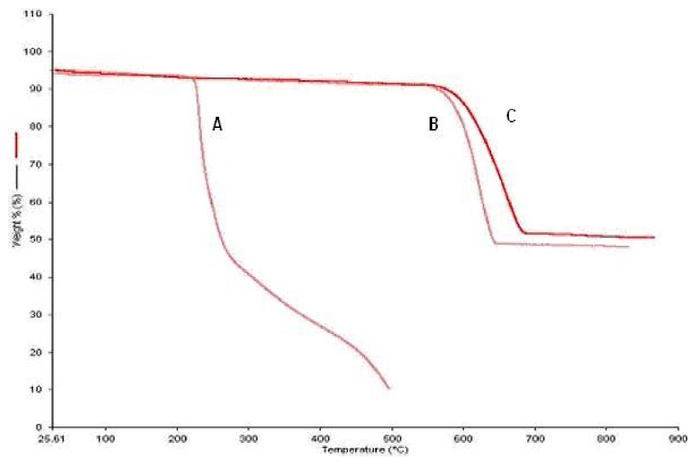
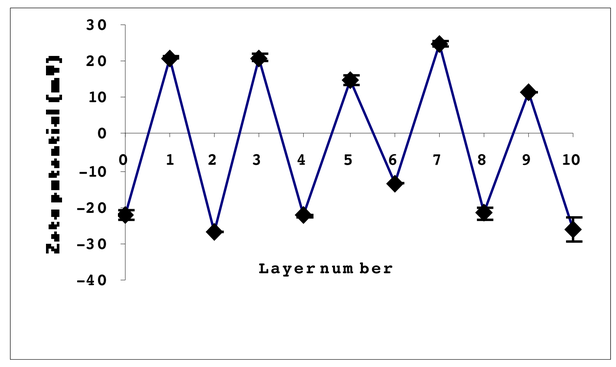
INTRODUCTION AND OBJECTIVE

Recently an extensive effort has been made in the development of smart, functional, organized delivery system by layer-by-layer (LBL) self-assembling technique for micro/nano-encapsulation of bioactives, Caruso [2001]; Decher and Schlenoff [2003]. The encapsulation of bioactive materials into porous microparticles of inorganic origin have a great potential to allocate the drug in their nanopores (nanoreservoir) and have features to impart biological stability along with sustained release properties. We have made an attempt to develop a novel formulation of paclitaxel (PTX) by providing multilayer assembly over drug loaded porous $CaCO_3$ microparticles ($CaCO_3$ MP) by using combination of biocompatible and biodegradable polyelectrolytes (PE' s). There has been a paradigm shift in the delivery of PTX and research being focused to eliminate intrinsic problem associated with drug itself and toxicity associated with excipients used in the existing formulation.

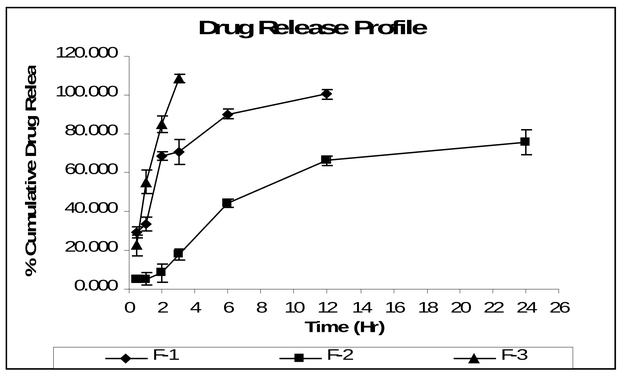


TGA curve of A. PTX; B. $CaCO_3$-PTX, and C. $CaCO_3$ MP.

LAYER-BY-LAYER GROWTH STUDY BY ELECTROPHORETIC MOBILITY

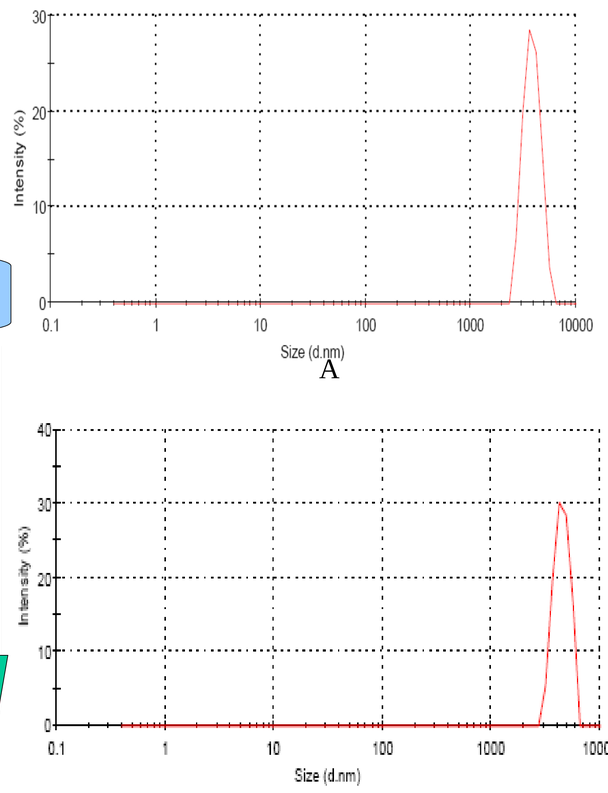


IN-VITRO RELEASE PROFILE



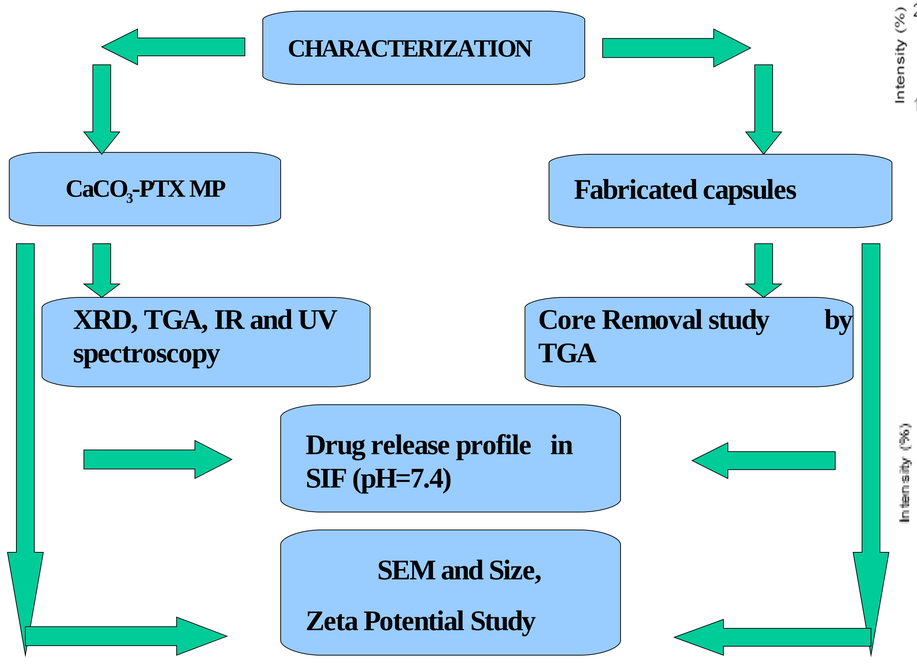
Drug release profile of formulations in SIF (pH=7.4): F-1:$CaCO_3$-PTX; F-2: PTX $(PRM/SA)_5$ and F-3: PTX-M.

SIZE AND SIZE DISTRIBUTION STUDY OF $CaCO_3$ MP AND FABRICATED CAPSULES

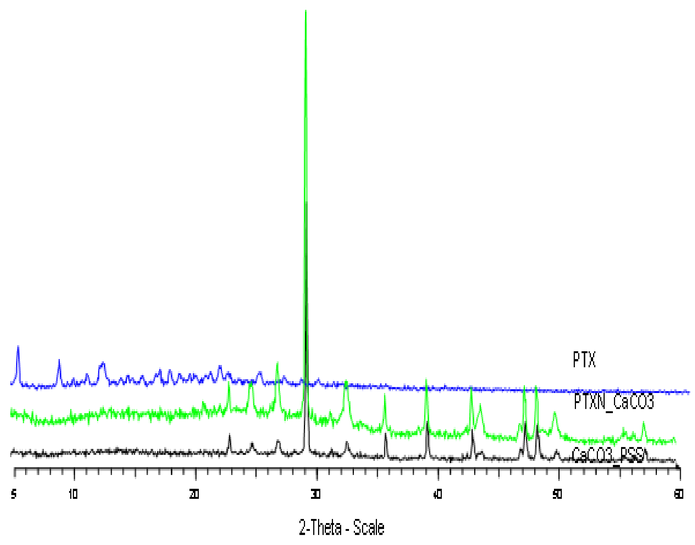


Mean particle size & size distribution of $CaCO_3$ MP (Average (d.nm):3558) and $CaCO_3$-PTX $(PRM/SA)_5$ (Average (d.nm):4110)

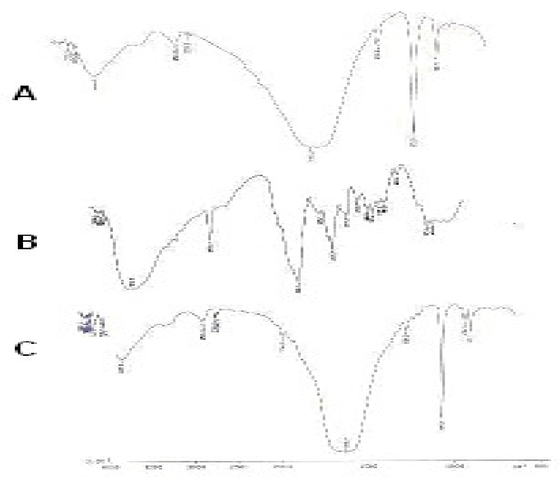
CHARACTERIZATION



POWDER XRD, TGA AND FTIR OF POROUS $CaCO_3$ MP, PTX AND $CaCO_3$-PTX

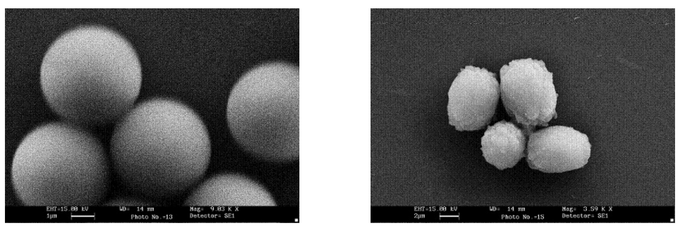


XRD comparison chart between PTX, $CaCO_3$-PTX, and $CaCO_3$ MP.



IR spectra of A. $CaCO_3$ MP B. PTX and C. $CaCO_3$-PTX.

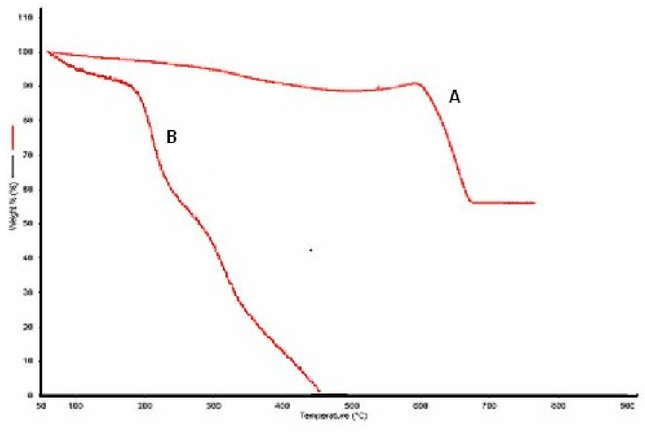
SEM OF POROUS $CaCO_3$ MP AND FABRICATED CAPSULES



A B

A: SEM of porous $CaCO_3$ MP
B: SEM of fabricated $CaCO_3$-PTX $(PRM/SA)_5$
Scale bar 1 μ m

CORE REMOVAL STUDY OF $CaCO_3$-PTX $(PRM/SA)_5$ BY TGA



TGA curve of A. $CaCO_3$-PTX $(PRM/SA)_5$, and B. PTX $(PRM/SA)_5$

DISCUSSION

- Nanoporous structure of inorganic decomposable core (charge substrate, $CaCO_3$) has been used for encapsulation of PTX and fabricated by LBL assembly of polyelectrolyte (PE' s) using electrostatic interaction due to its great importance in geo-, bio-, and material sciences, as well as due to its wide industrial, technological and drug delivery applications.
- Shape, surface morphology and narrow size distribution ranging from 4-6 μm of the $CaCO_3$ microparticles and fabricated capsules were presented by the particle size analyzer and SEM photomicrographs.
- Zeta potential study reveals layer-by-layer growth of the systems.
- The release profile of PTX-$(PRM/SA)_5$ indicates that PEs based multilayer matrix is capable to provide barrier to PTX release as it has been found to follow first order matrix diffusion kinetics (r2= 0.9973) with 72±4.8% release within 24 hrs. The $t_{50\%}$ of PTX-M, $CaCO_3$-PTX and PTX-$(PRM/SA)_5$ was found to be 70, 90 and 480 minutes respectively.

CONCLUSIONS

This alternative delivery system of PTX disguised in the form of LBL assembly could have been immense application for the treatment of metastasized mammary glands vis-à-vis existing formulation of PTX which is by and large criticized for having certain toxic excipients to be given parentrally. Further investigations are still underway to gather toxicity profile of the proposed formulation.

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