MANIPAL COLLEGE
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Development of Mesoporous Silica Nanoparticles for co-delivery of Tamoxifen Citrate and Resveratrol for breast cancer therapy

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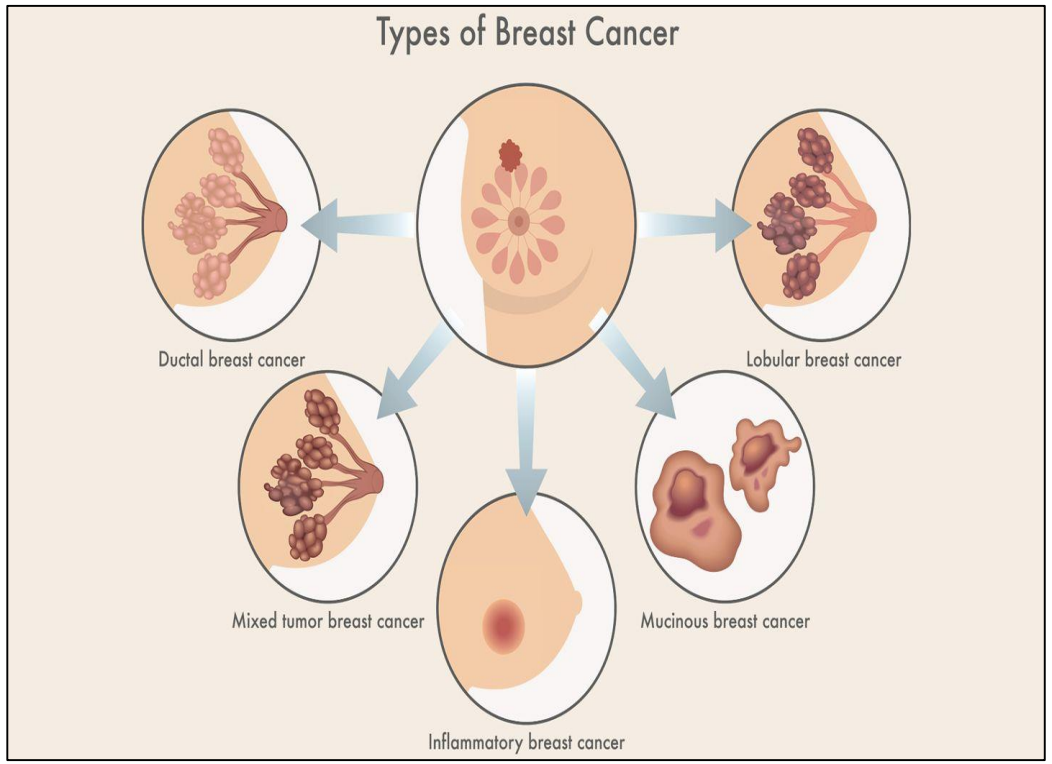
Introduction

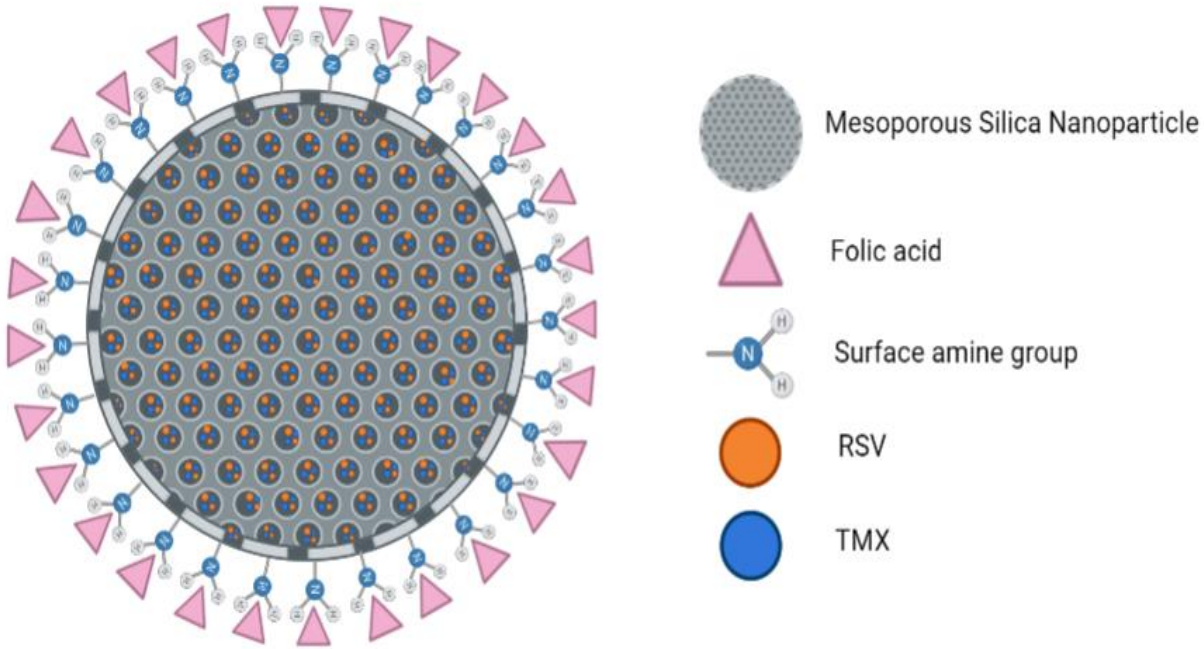
- Breast cancer in women: worldwide incidence rate of 31%
- Treatment of breast cancer involves a combination of surgery, radiation therapy and medication (chemotherapy/hormonal therapy/targeted biological therapy)
- Tamoxifen Citrate (TMX): an SERM, antiestrogenic and antitumor effects
- TMX is available as oral tablets (10mg/20mg) and oral solution (10mg/5ml) with a daily dose of 20 to 40 mg for 5 years



- Resveratrol (RSV) is a phytochemical which mediates anticancer effects, radical scavenging property
- RSV prevents formation of estrogen-DNA adducts, interferes with estrogen biosynthesis
- Both BCS class II drugs with limited aqueous solubility, hence limited oral bioavailability

Introduction

- **RSV-TMX combination:** synergistic activity by targeting multiple pathways, decreased incidence of resistance, re-sensitizes TMX resistant cancer cells to TMX
- Nanocarrier suitable for co-loading of multiple drugs → **Mesoporous Silica Nanoparticles (MSNs)**



- **Active targeting:** Folate receptor targeting by surface conjugation of MSNs with Folic acid, facilitates specific ligand-target interaction with the overexpressed folate receptors on the tumour cell surface

Aim and Objectives

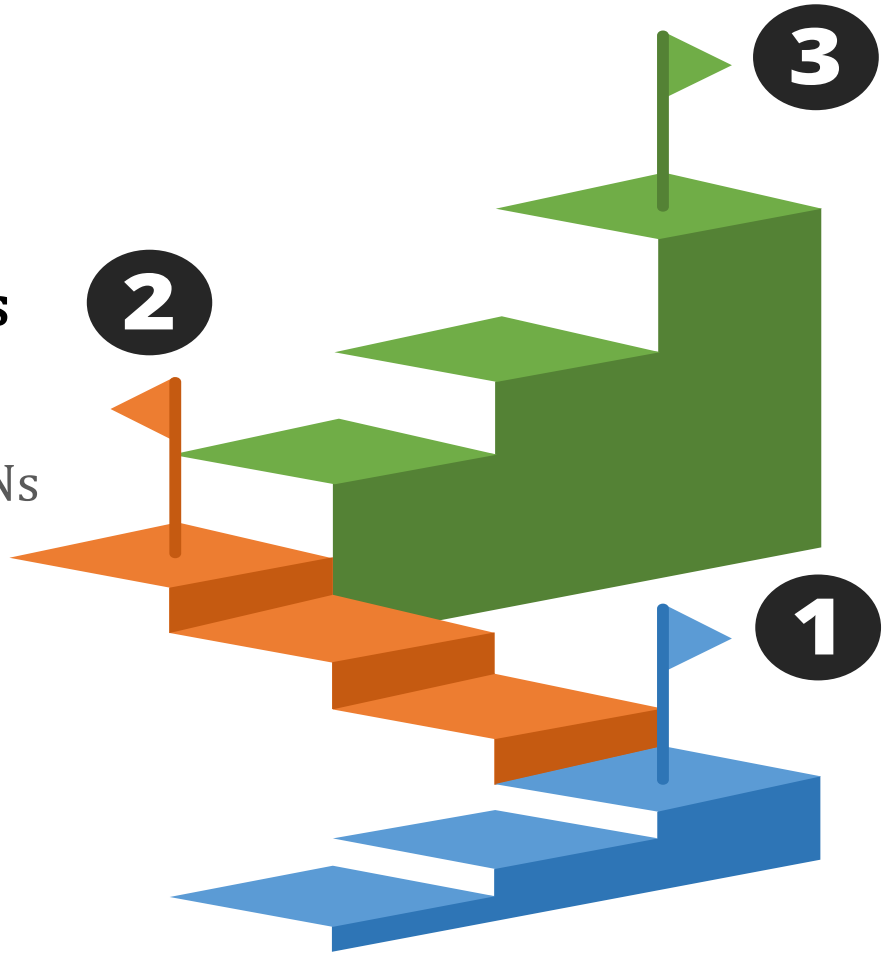
AIM:

To develop Resveratrol(RSV) and Tamoxifen Citrate(TMX) co-loaded Folic Acid conjugated Mesoporous Silica Nanoparticles (F-MSNs) for treatment of breast cancer

OBJECTIVES:

- To carry out pre-formulation studies for RSV and TMX
- To design, develop and characterize F-MSNs
- To design, develop and characterize RSV and TMX co-loaded F-MSNs

Methodology



Characterization of MSNs

FTIR
DSC
Particle Size & Zeta Potential
SEM
Drug Loading Capacity
Drug Loading Efficiency

Development of R-T-FA-MSNs

Preparation of MSNs

Amine Functionalization of MSNs (MSN-NH_2)

Folic acid Conjugation of Amine functionalized MSNs (F-MSN)

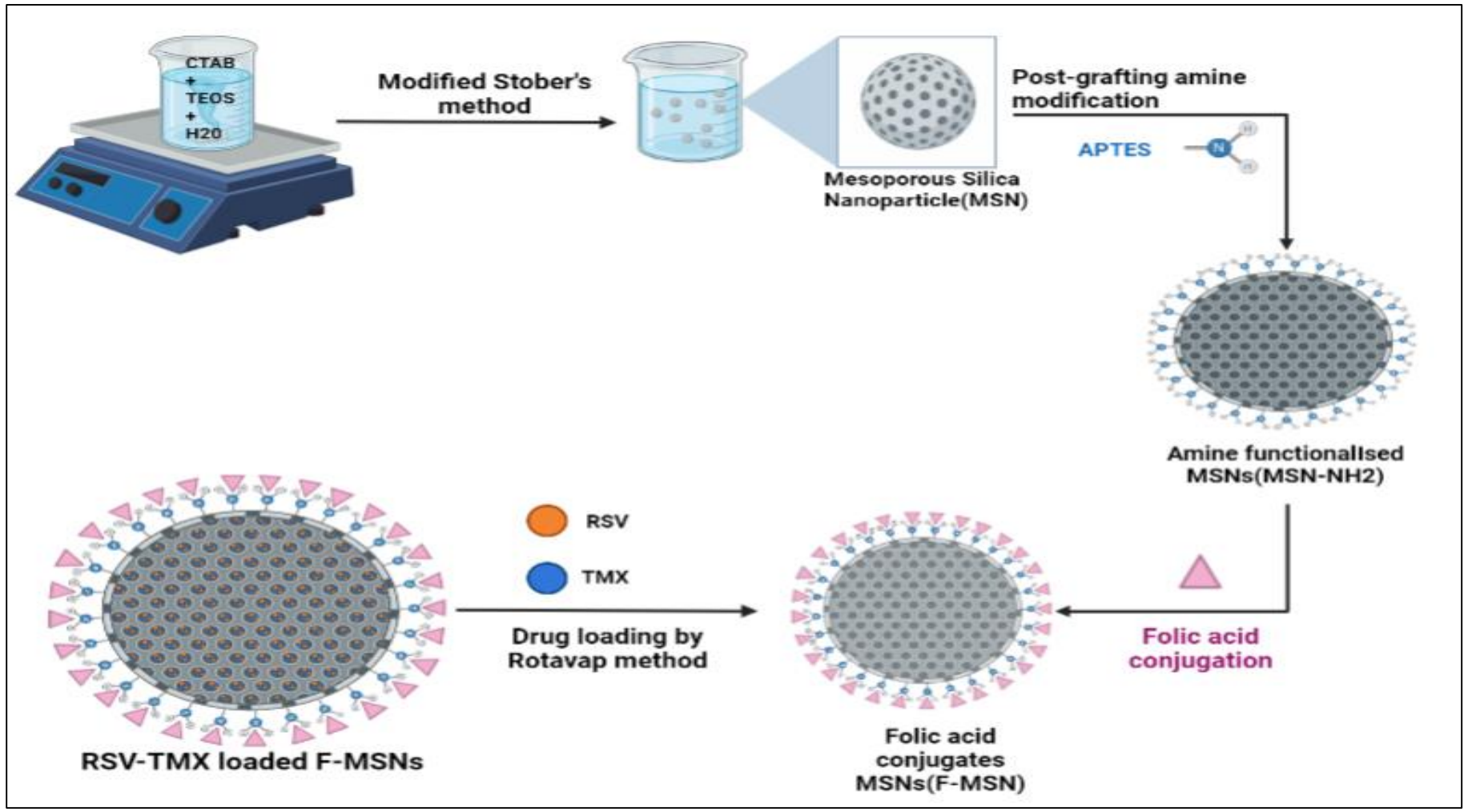
RSV and TMX Loading into FA-MSNs (R-T-F-MSNs) by Rotavap method

Pre-Formulation Studies

Development of Analytical method for RSV and TMX estimation – Vierodt's method

RSV/TMX-Mesoporous Silica Nanoparticle Compatibility Studies – FTIR & DSC

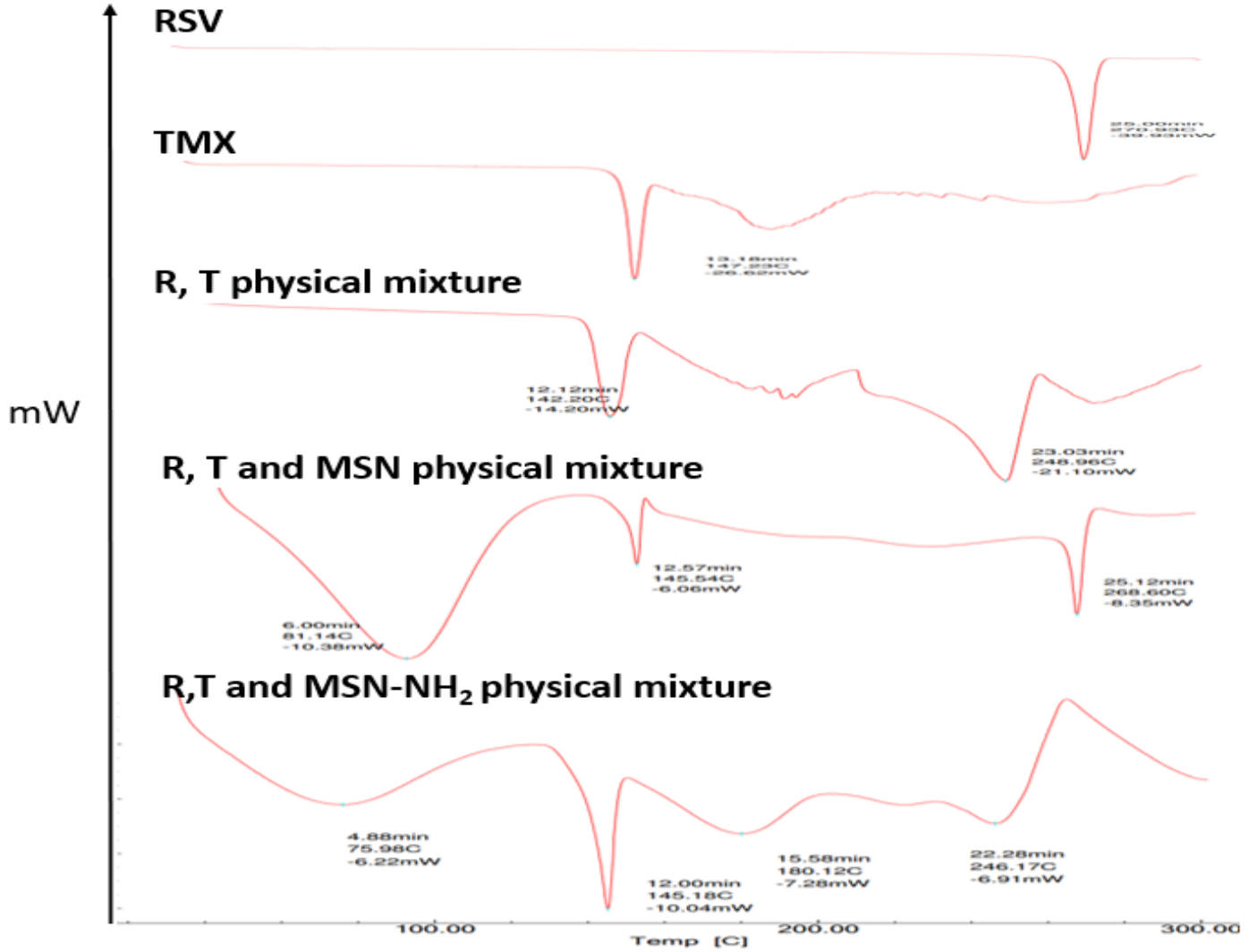
Methodology



Diagrammatic representation of development of RSV-TMX loaded Folic acid conjugated Mesoporous Silica Nanoparticles

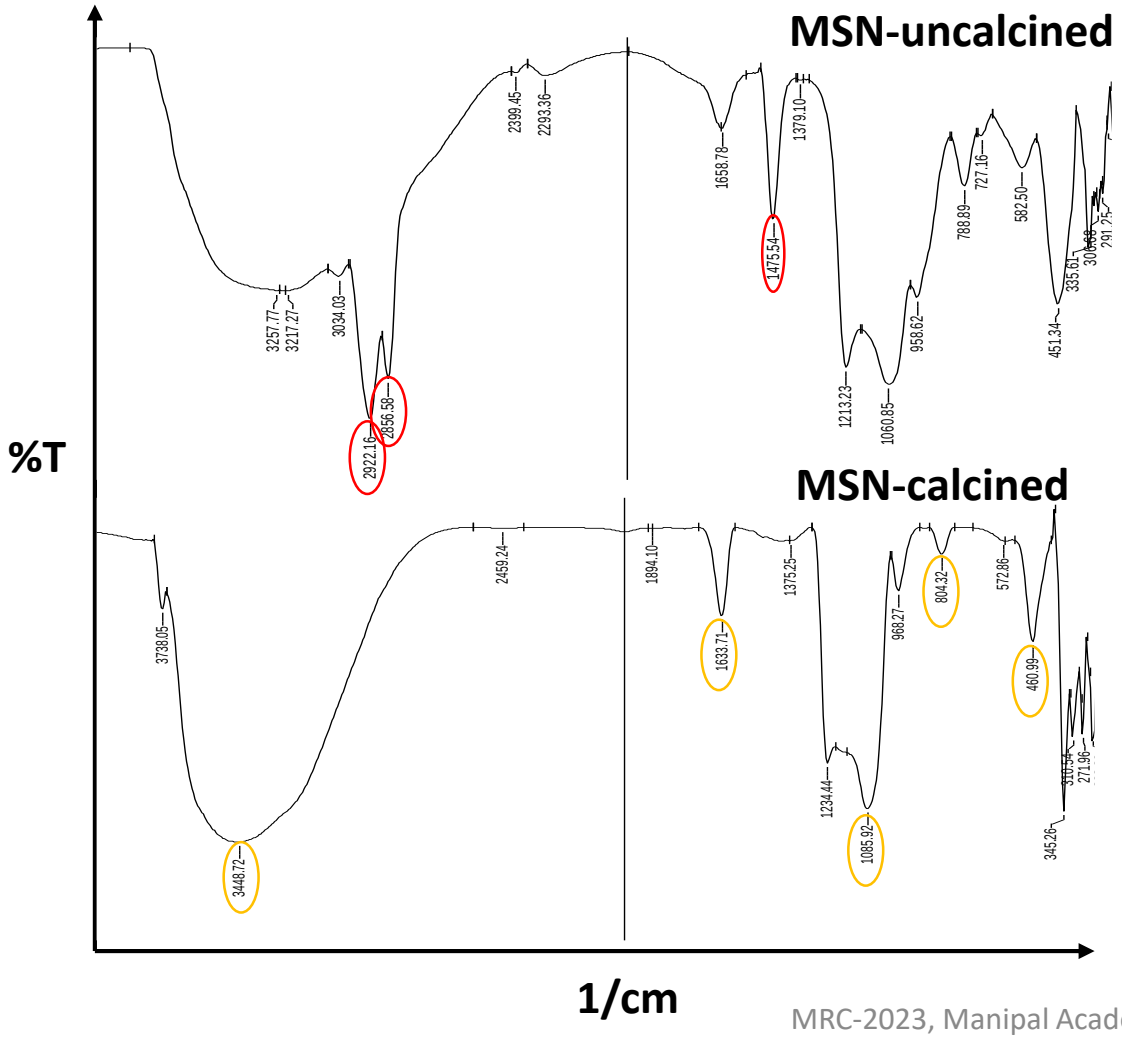
Results

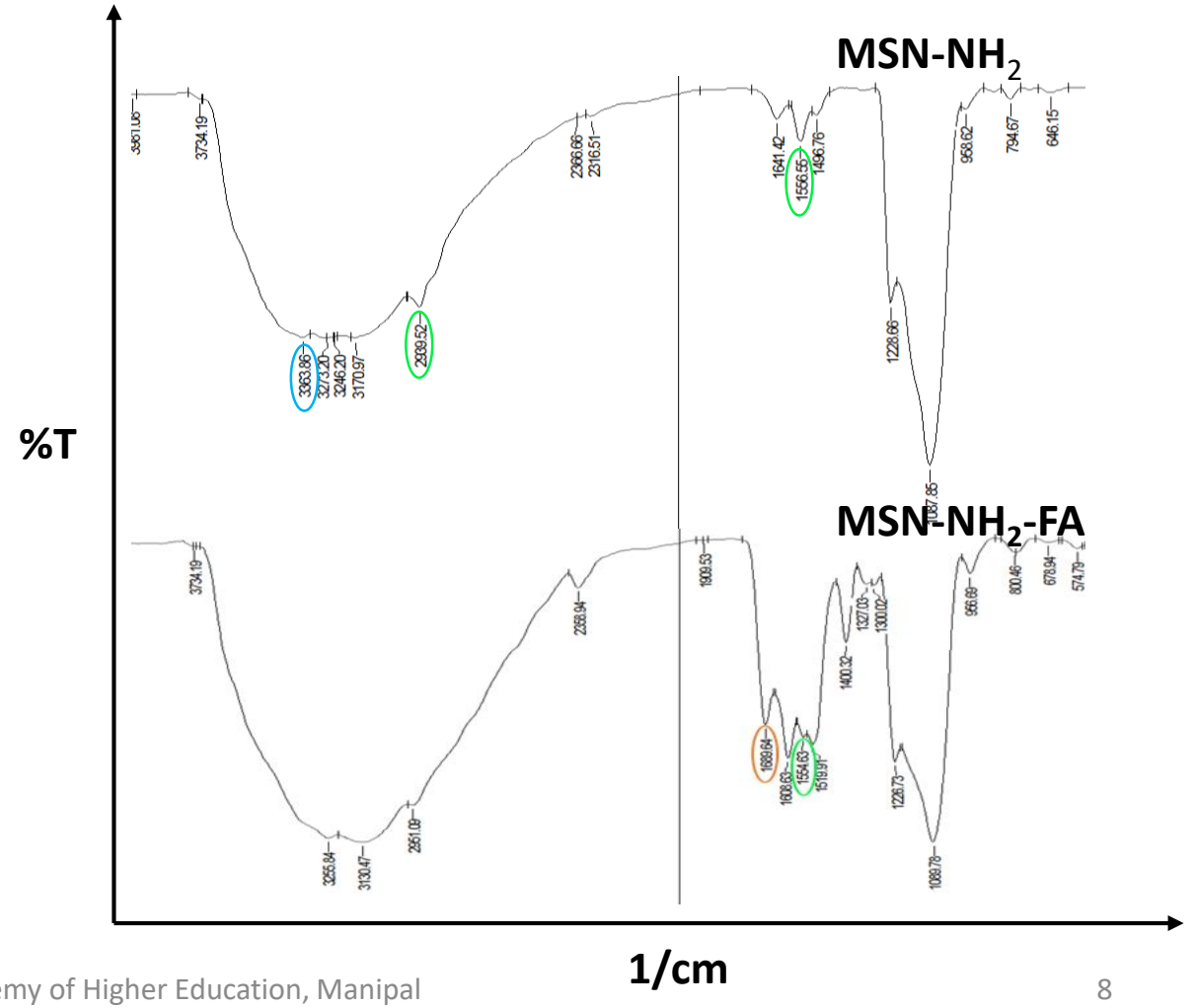
DSC studies to assess the compatibility between RSV, TMX and the developed MSNs



Results

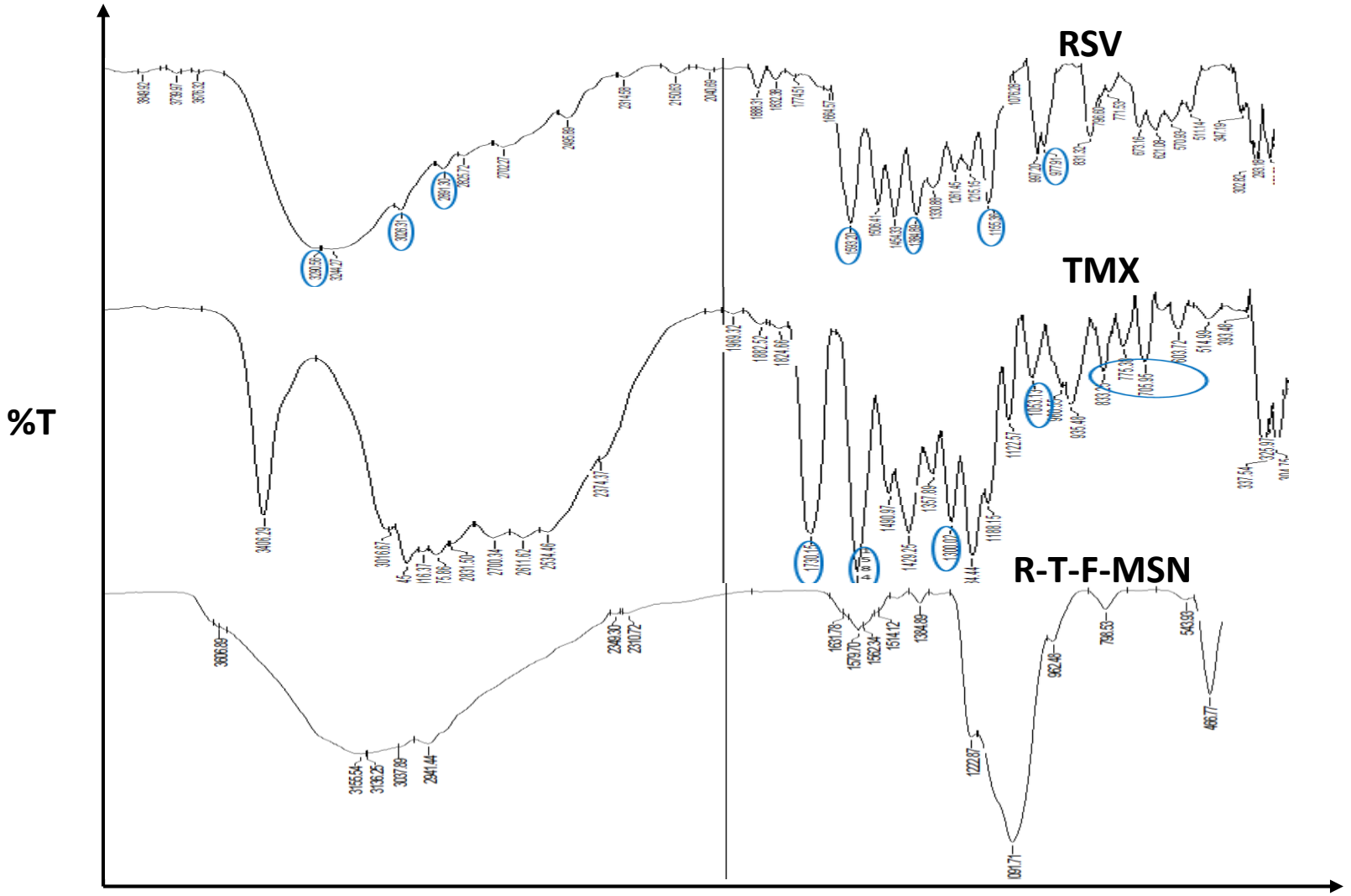
FTIR studies of developed MSNs





Results

FTIR studies of drug loaded F-MSNs

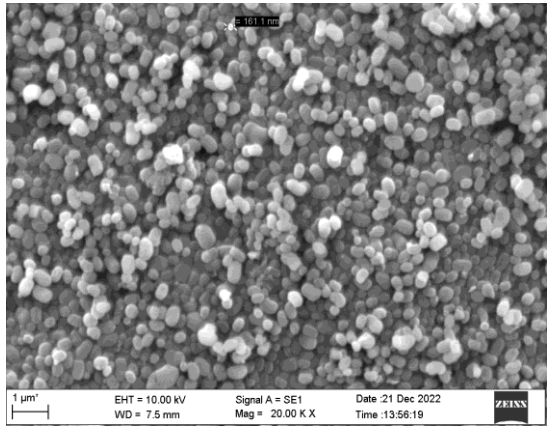


Results

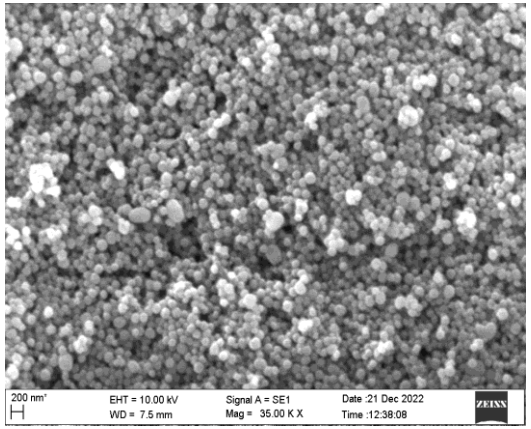
Drug Loading studies

Drug:MSN	Ratio	DLC(mg/g) of RSV	DLC(mg/g) of TMX	DLE(%) of RSV	DLE(%) of TMX
RSV:F-MSN	01:01	951.1 ± 2.12	-	95.11±0.21	-
TMX:F-MSN	01:01	-	738.8 ± 40.08	-	73.88±4.0
RSV:TMX:F-MSN	01:01:02	466.2 ± 3.53	363.3 ± 17.04	93.23±0.71	72.66±0.341
	0.8:01:02	367.09 ± 1.72	373.6 ± 0.19	91.77±0.043	74.71±0.038

SEM studies



MSN



MSN-NH_2

Particle size and Zeta Potential

Batch	Average size(nm)	Zeta potential(mV)
MSN	326±5.07	-24.9±0.38
MSN-NH_2	259±9.43	+42.4±0.23
MSN-NH-FA	295±7.6	-17.9±0.47

Conclusion

- MSNs, MSN-NH_2, F-MSNs, and co-loaded MSNs, were successfully synthesized and characterised
- Folic acid conjugation on the surface of the nanoparticle was achieved in order to explicitly target the folate receptor overexpressed tumour cells and to limit the uptake by normal healthy cells
- Loading of the combination of drugs into folate grafted mesoporous silica nanoparticles was achieved through Rotavap method, resulting in uniformly distributed, spherical and stable nano-sized particles

Our future work will be focused on evaluating the anticancer efficacy of these nanoparticles on breast cancer cell line and in animal models

The dual drug loaded formulation containing the antineoplastic agent Tamoxifen Citrate and the phytochemical Resveratrol, may help in reduction/reversal of Tamoxifen resistance in tumour cells, and provide therapeutic effects at significantly reduced doses, thereby minimizing the untoward effects

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THANK YOU