



*CHAPTER 3: AIMS AND
OBJECTIVES*

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3.1 Aims

- The main aim of the study was to formulate mesoporous silica nanoparticles for encapsulating selected anticancer drugs for their enhanced efficacy and improved properties such as dissolution rate and oral bioavailability enhancement of anticancer drugs Etoposide and Bicalutamide belonging to BCS class IV and II respectively.
- To study the surface functionalisation of MCM-41 MSNs for obtaining a targeted drug delivery system for ETO and BIC.

3.2 Objectives

The objectives of the study were

- To synthesize MSNs using with large surface area and optimum porosity properties
- To achieve a significant higher drug loading for synthesized MSNs utilising the unique properties of MSNs like large pore volume, pore size and high surface area using a suitable loading method.
- External surface functionalisation of MSNs based on a pH responsive and receptor based strategy.
- Achieving a more controlled release of drug in a sustainable manner specifically in case of surface functionalised MSNs.
- To achieve a targeting delivery of drugs with external surface functionalization of the MSNs by polyacrylic acid and folic acid which would aid their accumulation inside the cancerous cells by either passive or active targeting mechanism and eventually reduce the harm to healthy cells.
- To assess the cytotoxicity, pharmacokinetic evaluation and histological examination of MSNs for determining efficacy and safety.

- To develop a safe biocompatible MSN formulation.

3.3 Work plan

To achieve the desired objectives of the present study a workplan design given below was followed for both the drugs (Figure 3.1 and 3.2). An overview is given in figure 3.3.

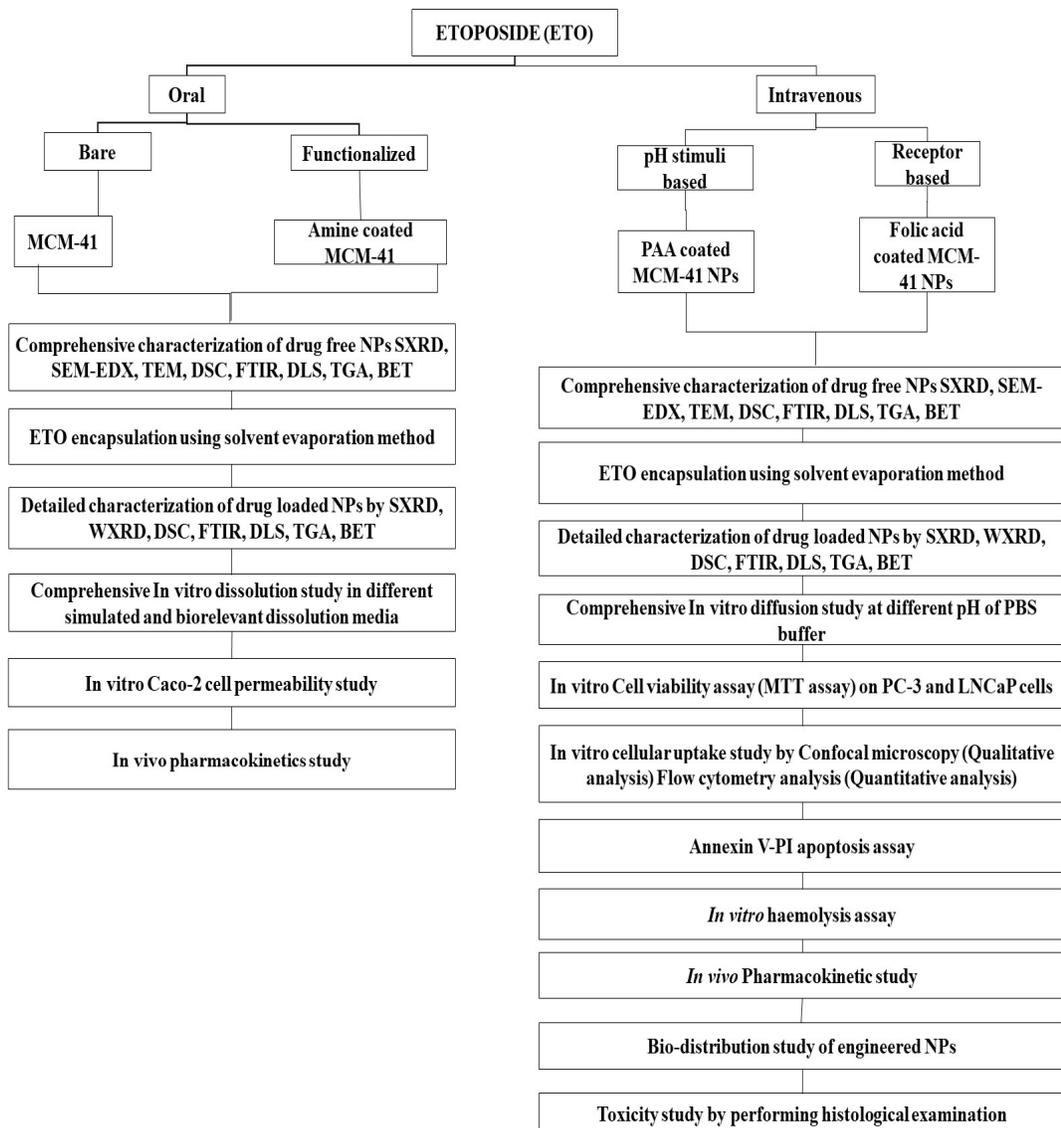


Figure 3.1. Schematic representation of work done for ETO

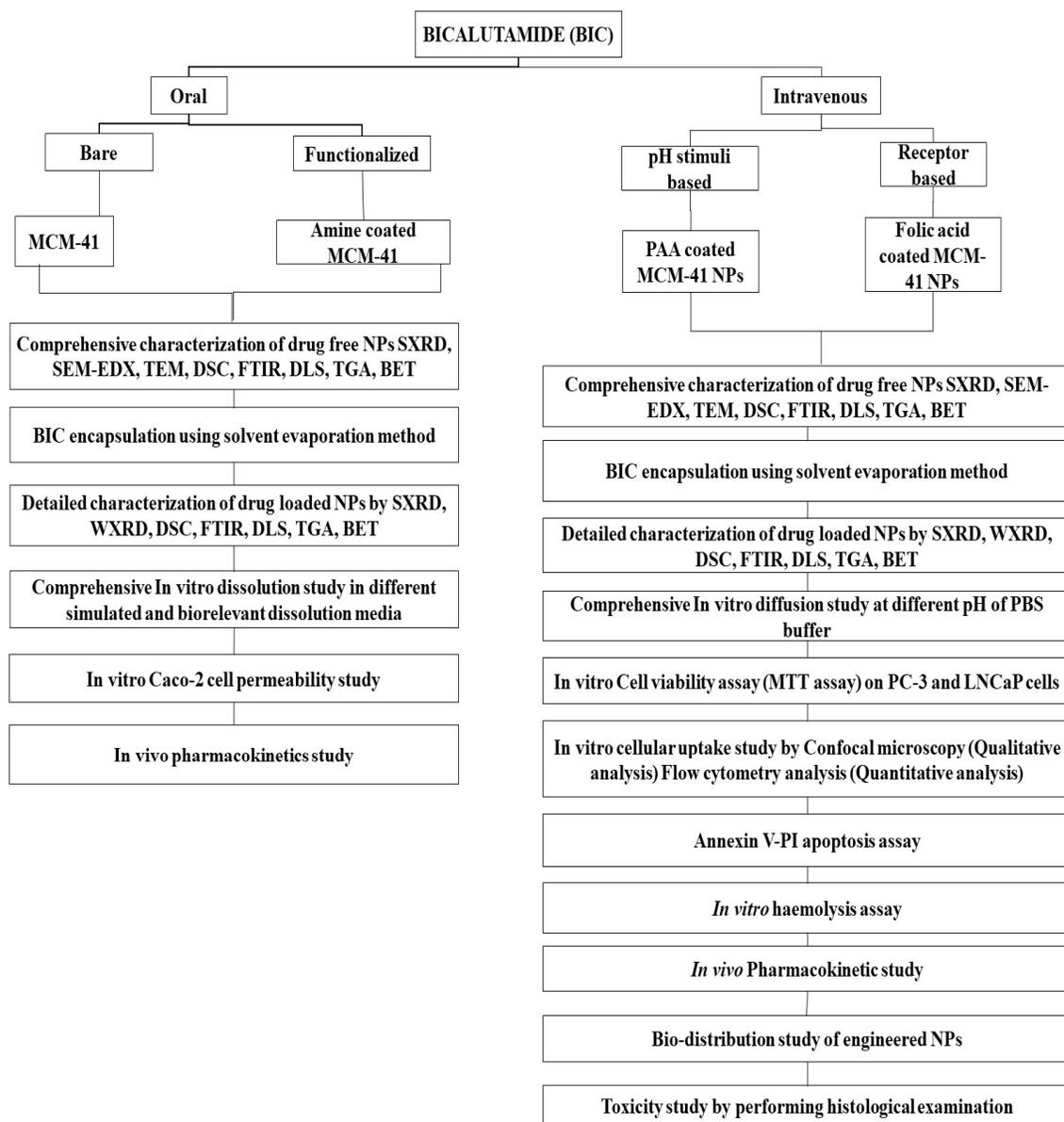


Figure 3.2. Schematic representation of work done for BIC

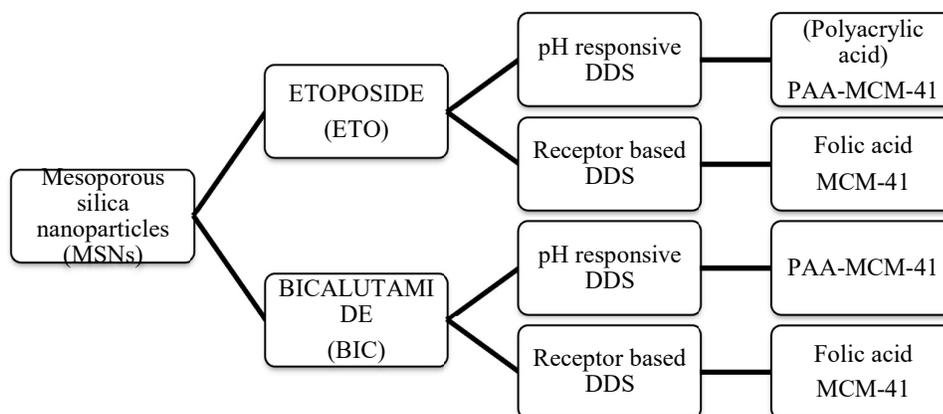


Figure 3.3 Overview of the formulations developed for ETO and BIC

3.4 Hypothesis

- It is hypothesized that the oral bioavailability of ETO and BIC would increase by encapsulating them into the mesoporous silica network. This would enhance their solubility and possibly permeability as well. This would further lead to enhancement in the oral bioavailability of both drugs.
- Cancer cells are distinct from normal cells in various aspects like having a more acidic pH, elevated GSH levels, overexpression of certain receptors in various types of cancer. It is reported that folate receptors are overexpressed in various tumours. Hence, it was thought of interest to synthesize MSNs which are surface coated with ligands such as folic acid and pH responsive moieties like poly acrylic acid which can aid in accumulating drug loaded MSNs at targeted tumour site. This would ultimately lead to anticancer drug accumulation exclusively at cancer site, thereby sparing normal cells. Additionally, the pH responsive and receptor-based targeting systems may also prove to be useful in minimizing the off-site harmful effects to healthy cells and organs.

- A more focussed targeted treatment using MSNs would lead to a reduction in therapeutic dose. This will minimize drug wastage. Most, importantly, reduction in dose leads to better efficacy and reduced side effects.

3.5 Expected outcomes

- It is expected that the surface functionalisation of bare MSNs would give a delivery system that would cause less haemolysis, and be more biocompatible at the same time serving the purpose of site specific delivery.
- An encasement of ETO and BIC in the mesoporous cage would have potential to enhance both the dissolution rate as well as the bioavailability which may prove to be helpful in the dose reduction and/or the frequency of drug intake.
- The surface modification by moieties like poly acrylic acid and folic acid, would aid the drug reaching exclusively to tumour cells and this could decrease the adverse effects of the anti-cancer drugs by minimizing the uptake by healthy cells.

The present study will provide an insight about the potential of silica nanoparticles as drug carriers. The surface functionalization and attachment of targeting ligand will ensure targeted delivery of the MSN to cancer cells. The present study will help in designing a suitable drug formulation for cancer cell targeting with increased therapeutic efficiency and decreased side effects. Targeted MSNPs will reduce the severity of disease and also lead to reduction in frequency or dose intake.