

Targeted Lung Cancer Treatment Using Etoposide-Conjugated MCM-41 Nanoparticles

^{1*} Om Prakash Yadav, ² Nitin Mittal

^{1*}Research Scholar, Faculty of Pharmacy, Lords University, Alwar, 301028, Rajasthan, India.

Email: ompharma096@gmail.com

²Professor, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Lords University, Alwar, 301028, Rajasthan, India. Email: mittalnitin1901@gmail.com

*Corresponding Author: Om Prakash Yadav**

Abstract

Mesoporous silica nanoparticles are seen as it is chemically stable and also showing thermal stability having very good porosity and morphological characteristic property. These particles having very good internal and external surfaces so that they can function with both the molecule either it is organic or inorganic. Silica is also very less toxic in nature so it is observed very best carrier for the nanotherapeutic delivery of the drugs to the body. The preparation of the silica nanoparticle was done with the Methanol (MeOH), Distilled water and Tetraethyl orthosilicate (TEOS) within the existence sodium hydroxide as catalyst and temperature at 80°C. Characterization through X-ray diffraction (XRD), In vitro release study haemolytic study and also cell line studies. Silica is good nanocarrier because of the no changes in the drug characteristics either structurally or chemically. It is showing desirable effect after release of the drug. The formulation shows very good effect of solubilisation of the non-hygroscopic nature of the drug Etoposide (ETP). The formulation shows good performance for the targeting delivery and also low toxicity profile with very higher rate of stability within the nano formulation.

Keywords: MCM-41, Mesoporous Silica Nanoparticles, Etoposide, Targeted Drug Delivery, Lung Cancer, Nanotherapy

How to cite this article: Yadav OP, Mittal N. Targeted Lung Cancer Treatment Using Etoposide-Conjugated MCM-41 Nanoparticles. *Int J Drug Deliv Technol.* 2026;16(10s): 838-841; DOI: 10.25258/ijddt.16.10s.98

Introduction

There are several critical factors to be considered when selecting a suitable carrier system. The carrier must be biocompatible in nature and should exhibit minimal or no premature drug release, thereby preventing unwanted drug leakage before reaching the target site. It should also possess tissue specificity or site-directing ability, ensuring targeted delivery. In addition, the carrier is expected to demonstrate high drug-loading and encapsulation efficiency, along with a controlled release profile to achieve the required local drug concentration at the desired site. Controlled drug delivery represents a highly promising approach in the advancement of chemotherapy[1,2]. It addresses several critical challenges in cancer treatment and significantly improves therapeutic outcomes. The field of nanotechnology has gained immense attention in recent years, attracting researchers worldwide due to its potential to overcome the limitations of conventional therapies. Nanocarrier-based systems offer multiple advantages, including reduced drug dosage requirements, minimized toxicity,

enhanced targeting ability, improved bioavailability, increased solubility, and stronger plasma protein binding capacity.

Materials and Methods

Cetyltrimethylammonium bromide(CTAB)(ottochemica purity $\geq 99\%$), Tetraethylorthosilicate(TEOS) (Alfaesar chemicals limited purity $\geq 98\%$), Ethanol(Mercpurity $\geq 99\%$), Dionised water, Sodiumhydroxide, Concentrated Hydrochloric acid, Polaxamer, Sodiumdihydrogen Orthophosphate dehydrate(Fisher scientific Purity $\geq 98\%$), Acetonitrile HPLC grade, Methanol(CDH purity 99.5%), Etoposide(ETP)(supplied as a gift sample).

Preparation method of Silica nanoparticles

The different amount of the silica nanoparticle was prepared by slight change in the process as reported by taking different concentration of CTAB (1.8 gm), 2.0 M Sodium hydroxide (1.9 mL), and water (100mL) putted it at 80°C for 30 min. when fully clear solution is observed then TEOS 2.3g is rapidly added with help of injection and rapid stirring nearly 600 rpm after

Targeted Lung Cancer Treatment Using Etoposide-Conjugated MCM-41 Nanoparticles

continuous stirring for four minutes there is observance of white precipitate the temperature maintained at 80°C for 2.5 hours. Then the product was diluted three times with distilled water nearly (300mL) and filtered simultaneously. Then it is washed with methanol and water solution in ratio (2:5) two times further its acid extraction was done with the methanol (100mL) conc. Hydrochloric acid (1mL) mixture and previously prepared sample nearly 1.3 g at 60°C for 6.5 h using hot plate. The resulted sample was then washed with water and methanol several time until all the surfactant(CTAB) were removed and then the solid product was collected by the centrifugation at 2000 rpm(CPR-30 Plus, REMI, India) The process was done with different concentration of the above used chemicals to obtain different types of the mesoporous silica nanoparticles MCM-NPs and the given table shows the concentration of the chemicals and name of sample obtained [3,4].

Sample Name	CTAB(g)	2.0M NaOH (mL)	H ₂ O(mL)	TEOS(g)
MCM-NPs-A	1.5	1.7	120	2.1
MCM-NPs-B	1.2	1.3	110	1.9
MCM-NPs-C	1.8	1.9	100	2.3
MCM-NPs-D	2.0	2.5	140	3.1

From the above prepared nanoparticle characterized and sample having given surface area i.e.MCM-NPs-A-540±2.5sq.m/g,MCM-NPs-B-630±3.2sq.m/g,MCM-NPs-C 720±1.9sq.m/g and MCM-NPs580±4.5sq.m/g in all these MCM-NPs-C providing large surface area which is good for the encapsulation of Etoposide[1].Successfully prepared MCM-NPs-Cwas confirmed with FT-IR.

Drug loading into silica nanoparticle - After confirmation through FT-IR sample nanoparticle MCM-NPs-C was loaded with Etoposide. It is done by the dissolving of etoposide 10mg into ethanol 6mL and then stirred unless homogeneous mixture is formed then dried MCM-NPs-C (50mg)was added to it and stirred for 20hrs at 400 rpm [5].

Powder X-Ray diffraction analysis

X-Ray diffraction of the solid nature of powder samples(ETP,MCM-NPs-C and MCM-NPs-C-ETP) was analysed with X-ray diffractometer(X'pert PRO, PANalytical B.V., Netherlands) enabled with CuK α target. The reported data was obtained at 2 θ diffraction angle 5⁰ to 50⁰ and the scanning speed was 4⁰/min radiation and having step size is 0.02⁰and X-rays was generated at the 40 mA and 45kV. the process of the analysis was repeated thrice to confirm appropriate results [6,7].

In vitro release study through High performance liquid Chromatography analysis

Liquid chromatograph Shimadzu LC-2010 CHT (M/s Shimadzu Co. Ltd., Chiyoda ku, Tokyo, Japan) equipped with 4.6 mm × 250 mm Merck HPLC column RP-18, ODS with particle size 5 micron and PDA detector with 284 nm wavelengths was used for the determination of in vitro release study. About the 5 mg of the sample MCM-NPs-C-ETP and 5 mg pure ETP was suspended in the 2mL of the 1% sodium lauryl sulphate (SLS) with phosphate buffer saline having pH 7.4 with cellulose membrane of fixed cut off (MW cut-off 5000, Hi-Media) separately. The dialysis bags were placed in 50 mL of the phosphate buffer saline(7.4pH) solution (sink condition) with magnetic stirring at 75rpm and then 1.5 mL aliquots was extracted at different time intervals and replaced with fresh buffer solution of same amount 1.5mL and after 24 hrs the sample was analysed with reverse phase HPLC C₁₈ column (Arumugam et al., 2011, Jambhrunkar et al., 2014Pencheva et al., 2008). The used solvent was carbinol of HPLC grade with water of HPLC grade and acetonitrile of HPLC grade (50:50:80 v/v) and before using it was filtered with membrane filter of 0.22 μ m and flow rate was maintained 1mL/min the experiment was revised double time for the analysis of variability obtained with each time. The obtained chromatogram was analysed further.

Ex vivo study

Percentage live red blood cells (RBC) count study

As per suggested protocol percentage live RBC was calculated by subtracting the percent haemolysis from the total haemolysed sample i.e., haemolysis by distilled water the percentage of live blood cells was calculated of samples naïvedrug ETP, blank MCM-NPs-C and final loaded drug MCM-NPs-C-ETP. Human blood sample was calculated from the healthy human 8 mL within the EDTA storage vial and then the blood sample was centrifuged at 2500 rpm (R-4C DX, REMI, India) and then the RBC was collected and instantly suspended into

Targeted Lung Cancer Treatment Using Etoposide-Conjugated MCM-41 Nanoparticles

normal saline solution (0.9%w/v). Then sample which should be analysed prepared of (20ppm) and placed 4mL each samples and then equal amount of RBC are placed to each samples and let it for the incubation period of the 30 minutes and after incubation it was centrifuged and supernatant was analysed as it is by ultraviolet visible spectrophotometer(Cary series-100, UV-visible spectrophotometer, AgilentTech.)(Khan et al.,2007 Agarwal et al., 2007,Singhai et al.,1997). RBCs in distilled water considered as 100 percent haemolysis or no live RBCs left and the absorbance of distilled water is taken as a reference for other samples

$\% \text{ RBC Live} = \frac{\% \text{ haemolysis DW} - \% \text{ haemolysis of Samples}}{\% \text{ haemolysis DW}} \times 100$

For $\% \text{ Haemolysis} = [a_s \div a_{100}] \times 100$

Where a_s =absorbance of sample

a_{100} = absorbance of distilled water

In the above report time dependent percent RBCs live are counted i.e., 30 minutes, 12hours and 24 hrs respectively.

Protein binding study

A Solution of BSA was prepared (2% w/w) of PBS saline of pH 7.4 for the study. ETP (1mg) and MCM-NPs-C-ETP (equivalent to 1 mg drug) were added to 1 mL of BSA solution and packed into dialysis bags, separately. These dialysis bags were dipped into 20 mL of PBS of pH 7.4 under stirring at 37 ± 1 °C. Samples were analyzed spectrophotometrically which were taken at the intervals of 1 h, 2 h, 3 h, 4 h, 5 h and 6 h. The calculations of percent protein drug binding were performed, as per the equation (weser et al., 1976, Singh A et al.,2016).

$$\% \text{ Protein drug binding} = \frac{(\text{Theoretical amount of drug in bag} - \text{Drug in sink})}{\text{Theoretical drug in bag}} \times 100$$

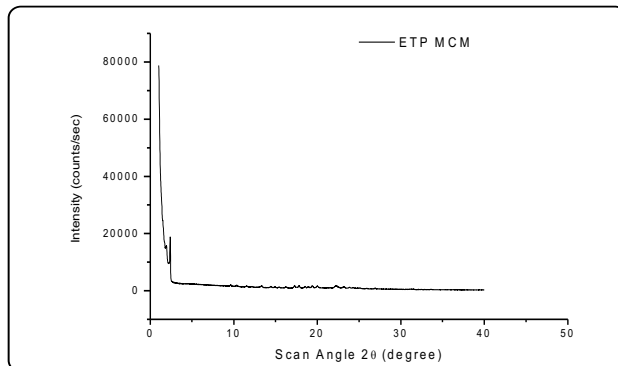
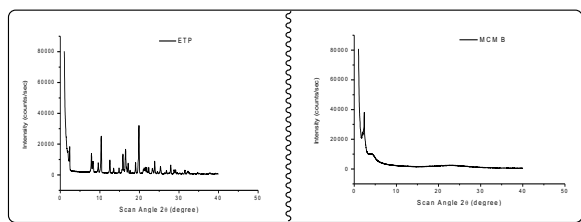


Figure 5: Powder XRD pattern ETP, MCM-NP-C blank and drug loaded silica nanoparticles i.e., MCM-NP-C-ETP.

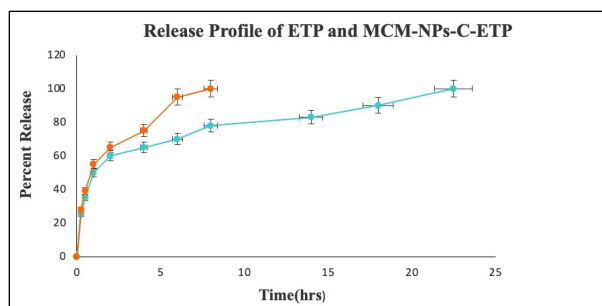


Figure 6: In vitro release profile of the pure drug ETP, MCM-NP-C-ETP.

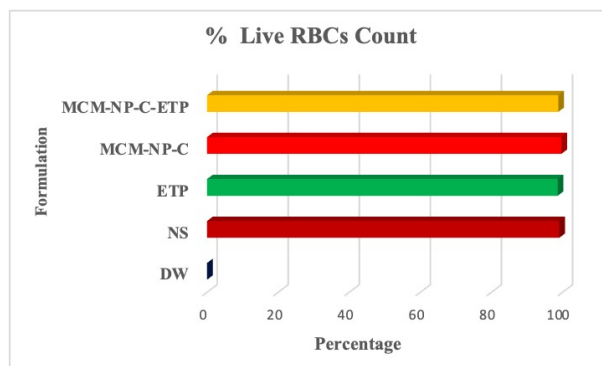


Figure 7: Percent live RBCs count in DW, NS, ETP, MCM-NP-C, MCM-NP-C-ETP.

Targeted Lung Cancer Treatment Using Etoposide-Conjugated MCM-41 Nanoparticles

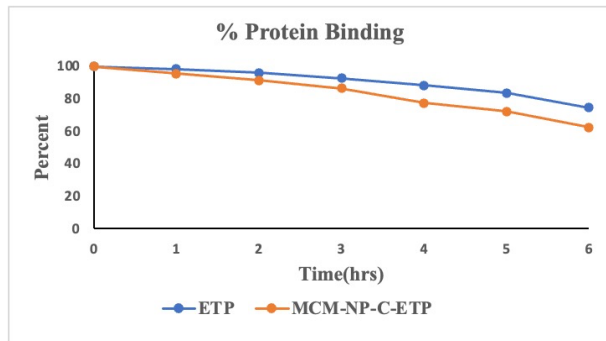


Figure 8: Protein binding study of the pure drug ETP and MCM-NP-C-ETP.

Conclusion

Etoposide-loaded mesoporous silica nanoparticles were successfully developed and thoroughly evaluated for their potential in lung cancer drug delivery. XRD analysis confirmed the preservation of mesoporous structure and effective drug incorporation within the silica framework. The release study demonstrated a controlled and sustained drug release profile, highlighting the suitability of the carrier system for maintaining therapeutic concentrations. Protein binding studies indicated favorable interactions that may prolong systemic circulation and enhance drug bioavailability. Furthermore, hemolytic toxicity assays confirmed the biocompatibility of the formulation, with minimal red blood cell damage observed. Collectively, these findings establish etoposide-loaded mesoporous silica nanoparticles as a safe and efficient nanocarrier system for targeted lung cancer therapy.

1. Jambhrunkar S, Qua Z, Popat A, Karmakar S, Xu C, Yu C. Modulating in vitro release and solubility of griseofulvin using functionalized mesoporous silica nanoparticles. *J Colloid Inter Sci.* 2014; 434: 218–225.
2. E. Pencheva, A. Bogomilova, N. Koseva, D. Obreshkova, K. Troev, HPLC study on the stability of bendamustine hydrochloride immobilized onto polyphosphoesters, *J. Pharm. Biomed. Anal.* 48 (2008) 1143–1150.
3. Khan I, Gothwal A, Sharma A. Biodegradable nano-architectural PEGylated approach for the improved stability and anticancer efficacy of bendamustine. *IntJourn of Bio Macr.* 2016; 92: 1242–1251
4. Agarwal P, Gupta U, Jain NK. Glycoconjugated peptide dendrimers-based nanoparticulate

system for the delivery of chloroquine phosphate. *Biomaterials.* 2007; 28: 3349–3359.

5. A.K. Singhai, S. Jain, N.K. Jain, Evaluation of an aqueous injection of Ketoprofen, *Pharmazie.* 1997; 52: 149–151
6. Koch-Weser J, E.M. Sellers, Binding of drugs to serum albumin (first of two parts), *N. Engl. J. Med.* 1976; 294: 311–316.
7. Singh A, Thotakura A. PLGA-Soya lecithin based Micelles for Enhanced Delivery of Methotrexate: Cellular Uptake, Cytotoxic and Pharmacokinetic Evidences. *IntJourn of Bio Macr.* 2016; 11: 111.