Synthesis and Characterization of Mesoporous Silica MCM-41 and its use as Potential Drug Carrier

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Abstract

In developing countries to control viral and microbial infections, it is one of the biggest challenges to develop a resistance against antiviral and anti-microbial. This study was aimed at drug-loaded mesoporous silica nanoparticles (MSN) with ciprofloxacin and daclatasvir. Drug- loaded mesoporous silica nanoparticles were prepared & studied their releasing properties. The prepared materials were characterized by "Fourier- transform infrared spectroscopy (FTIR), "nitrogen adsorption/desorption analysis, and scanning electron microscopy" (SEM). Nanoparticles were loaded with drugs ciprofloxacin and daclatasvir for 24 hours which shows percent loading as 38.7% and 45.5% respectively. The results show that separate and distinct profiles were observed for both drugs. The MCM-41 loaded with Daclatasvir shows a faster rate of drug release compared to MCM-41 loaded with Ciprofloxacin. The finding suggests that MCM -41 could be a potential drug carrier system for controlled and extended release of antiviral and microbial drugs to enhance the drug efficiency to heal and treat infectious diseases. The release profile of both drugs was studied for 24 hours in vitro drug release.

Keywords: Mesoporous Silica, Potential Drug Carrier, Scanning Electron Microscopy,

Introduction

Significant development in medication delivery technologies during the past few decades have made drug administration more efficient. A wide range of organic systems, including "micelles, liposomes, and polymeric nanoparticles", have been developed to transport medications to organs. They have drawbacks, such as low thermal and chemical stability, and quick immune system removal. Silica particles, on the other hand, present a stable, "stealthy" option that is biocompatible. "By combining sol-gel polymerization with either spray- drying or emulsion chemistry", bioactive compounds can be conveniently encased within silica particles Spray-drying encounters difficulties such as limited yields, surface segregation, and size restrictions. In contrast, sol-gel emulsions allow for ambient temperature processing, which is required for handling biologicals, and the creation of nanoparticles with uniform drug dispersion. It is simple to gain independent control of the size and release rate. [1]. Initial in vivo tests demonstration that the nanoparticles are blood stable, and when combined with the prolonged release of anti- tumor drugs, they have good potential as a cancer treatment. [2] This rapidly expanding sector calls for interdisciplinary research, offers design options, and enables the creation of multifunctional devices that can target, identify, and treat fatal conditions like cancer. [3] Mesoporous silica nanoparticles (MSNs) have gained more and more attention in the last 10 years because of their potential for use in biomedicine. Compared to conventional drug nanocarriers, MSNs as drug delivery systems (DDSs) exhibit substantial benefits due to their customized mesoporous structure and high surface area. [4, 5] Post-grafted MCM-41 with organic functional groups 3-aminopropyl trimethoxy silane (APTMS) and 3-chloropropyltriethoxysilane (CPTMS), and L-tryptophane covalently linked to organic grafted chains for better physicochemical properties of mesoporous silica and controlled delivery. The release study of amoxicillin shown to be 12.9 wt. % and 33.0 wt. % loaded amoxicillin could be released from APTMS treated MCM-41 and pure MCM-41 after 24 h, however, 41.0 wt. was released from CPTMS treated MCM-41 after 24 h. When the post grafted samples were further modified with L-tryptophane, the slower release rate was attained. Similar materials with ibuprofen loading, synthesized via both post-grafting and co-condensation methods for MCM-41. Their results suggested that drug release may be well modulated by altering the grafted organic groups.[6] Thomas Bein and colleagues investigated the bio-degradation behavior of several functionalized mesoporous silica nanoparticles made in a single pot. The plain MSNPs, chloropropyl-, amino propyl-, phenyl-, and PEG-modified MSNPs were kept in simulated body fluid (SBF) for one month, also evaluated for the deposition of hydroxyapatite on the surface of samples. Phenyl- modified MSNPs show the highest degradation rate where PEGylated nanoparticles exhibited the lowest rate of degradation. [7, 8] Mesoporous nanoparticles are promising delivery systems for the extremely toxic medications such as chemotherapeutic agents, anti-infectives, antivirals, and anti-inflammatory medicines. Therefore, our goals include developing a sustained drug delivery system and evaluating the kinetics of the drug release from that system .[9, 10]

Experiment

Tetraethyl ortho silicate (TEOS), Ciprofloxacin, Daclatasvir, Hydrochloric acid, Monobasic potassium phosphate, "Sodium hydroxide, Sodium chloride, Potassium chloride, Sodium phosphate dibasic" and Ammonium hydroxide are obtained from Sigma-Aldrich, "Cetyltrimethylammonium bromide ($CH_3(CH_2)_{15}N(Br)(CH_3)_3$)" from Avon Chem, Ethanol from BDH, and Phosphate buffer saline tablets are obtained from Bio-World were used in this work.

Methodology

Synthesis of Mesoporous Silica

To synthesize the MCM-41 basic hydrolysis method was used, which is known as a solgel process. At room temperature, surface directing agent, 19.21mmol (7.0gram) of cetyltrimethylammonium bromide (CTAB) was added to a hydroalcoholic solution containing 150cm^3 of distilled water and 135cm^3 of ethanol in a 1000cm^3 round bottom flask. Further, add 39cm^3 of ammonium hydroxide to a mixture in a round bottom flask. It is kept vigorously stirring for 30min or until a clear solution is obtained. Then add, drop wise 54.80mmol (13.09ml) of a silicon source, for example, TEOS. Subsequently, white precipitation was seen after 5min of stirring. The reaction temperature and stirring conditions were sustained for additional 2hours. The finished product was filtered, collected, and then washed with water and ethanol before being dried under reduced pressure. The material is designated as MCM-41 + CTAB [11, 12]. The dried powder was subjected to calcination at 773-823K for the removal of surfactant with the heating rate of 275K per minute and held for 5 hours. The material is assigned as MCM-41 after sintering [13, 14].

Drug Loading

To encapsulate the therapeutic agent, ciprofloxacin (Cipro) about 0.010g of mesoporous silica was soaked in a 10 cm^3 aqueous solution of ciprofloxacin, having a drug strength of 0.001g/dm. After soaking for 24hrs in falcon tubes, loaded material was centrifuged at 16000rpm for 10min. To get rid of any loosely bound drug to a mesoporous carrier, distilled water was used to wash the medicine-loaded nanoparticles of mesoporous silica. Later the drug-loaded silica was dried under vacuum. The supernatant was collected to analyze the remaining drug concentration using a UV-Visible spectrophotometer at 257nm.[15, 16]

To encapsulate the second therapeutic agent, daclatasvir (Decla) about 0.01g of each mesoporous silica nanoparticulate carrier was soaked in a 10 cm^3 ethanol solution of declatasvir, having drug strength of 0.001g/dm. After soaking for 24hrs in falcon tubes, loaded material was centrifuged at 16000rpm for 10min. The drug-loaded nanoparticles of mesoporous silica were washed with ethanol to remove any loosely bound drug to a mesoporous carrier.[17, 18] Later the drug-loaded silica was dried under vacuum. The supernatant was collected to analyze for the remaining drug concentration using a UV-Visible spectrophotometer at 317 nm.

Evaluation of Drug Loading concentration:

The following formula was used to assess drug loading (DL).

Drug Loading (DL) = $(Qt_{otal}\ {}_{-}Su_{pernatant)} / Qt_{otal} \times 100$

Where Q $_{\text{total}}$ and Q $_{\text{supernatent}}$ correspond to the initial drug concentration in loading solution and drug quantity in the supernatant after loading.

In Vitro Drug Release:
An automatic USP-II test was performed for the release of drug in vitro research 100 mg of the mesoporous silica loaded drug was added into the vessels containing dissolution medium i.e., 900 ml of PBS and 900ml of 0.1N HCL solution. After the regular interval, 4ml of the solution was aliquot and then 4ml of the fresh solution was added. The temperature was kept up at 37^0C. The vessel was continually stirred with the help of a paddle at 50 rpm during the whole experiment, and the dissolving medium's temperature was maintained at 37 ± 0.5 °C. The drug release was investigated at 257nm for ciprofloxacin and '317nm for daclatasvir utilizing a UV-visible spectrophotometer [19].

$$Concentration\ of\ drug = \frac{absorbance - y - intercept}{slope}$$

Results and discussion

Energy Dispersive Spectroscopy

Hexagonal porous nanoparticles of MCM-41was successfully produced. The best template removal technique was used to remove the surfactant. Different characterization techniques confirm the incorporation of a functional group on mesoporous silica. An analytical method for biochemical characterization or elemental analysis of the material is energy dispersive spectroscopy (EDS). To obtain the percentage of the elements which are chemically bonded to inorganic silica network energy dispersive spectroscopy is performed. The percentage of each element found in MCM-41 is sum up in table 4.1. The EDS of MCM-41 shows the presence of Si weight % =19, C weight % =40.38, O2 weight %=36.3 and N weight % =4.3, a small percent of nitrogen is the remains of ammonium hydroxide used as a catalyst.[20, 21]
The percentage of each element found in MCM-41 is summed up in table 4.1. The energy dispersive spectroscopy EDS of MCM-41 shows the presence of silicon Si weight % = 19, carbon C weight % = 40.38, oxygen O2 weight % = 36.3 and nitrogen N weight % = 4.35.
Table 1. Relative percentages of elements present in mesoporous silica MCM-41

Weight Percentages of Elements					
MATERIALS	**Silicon**	**Carbon**	**Oxygen**	**Nitrogen**	**Chlorine**
MCM-41	19.06%	40.385%	36.35%	4.35%	0%

Nitrogen Adsorption Desorption Analysis

Textural parameters of MCM-41 such as surface area pore size, pore-volume, and nanoparticle size is given in table 4.2. The surface area of MCM-41 is calculated according to Brunauer–Emmett–Teller theory while pore size, and pore volume are determined according to BJH (Barrett-Joyner-Halenda) analysis[22]. The BET surface area of MCM-41 is 69.3656 m^2/g. The pore size of material obtain from BJH analysis is 19.3724 A and the pore volume is0.033594 cm^3/g. The nanoparticle size of MCM-41 is 86.4983 nm. Due to the material's vast surface area, a high concentration of medication may be adsorbed on its surface. The BET surface area of MCM-41 is 69.3656 m^2/g. The pore size of material obtained from BJH analysis is 19.3724 A and the pore volume is 0.033594 cm^3/g. The nanoparticle size of MCM-41 is 86.4983 nm.

Table 2. The textural parameter of synthesized mesoporous silica MCM-41.

Sr #	**Materials**	**Surface Area (BET) m^2/g**	**Pore size Å**	**Pore volume cm^3/g**	**Particle size (nm)**
1	MCM-41	69.40	19.40	0.034	86.50

X-Ray Diffraction Analysis.

Figure 4.1 depicts MCM-41's XRD pattern. In XRD spectra, mesoporous MCM-41 appeared amorphous. Long-range order exists, but no obvious peak is seen. An analytical method for identifying a crystalline materials phase that can reveal details about unit cell dimension is X-ray diffraction. [23, 24]

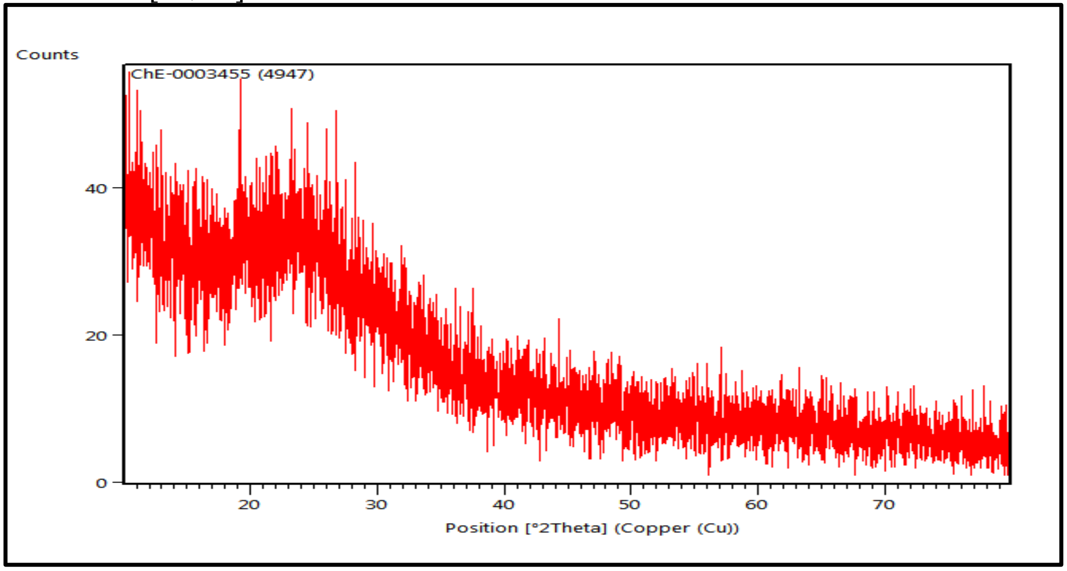

Figure 4.1 X-ray Diffraction analysis of Mesoporous silica MCM-41.

Infrared spectroscopy

Characteristic bands associated with the siloxane backbone of mesoporous silica MCM-41 are shown in figure 4.2. Broadband observed in 3500-3000 cm-1 range is due to the stretching of free silanol groups (Si-OH). A sharp peak at 1055 cm^{-1} was detected which is typical for asymmetric Si-O-Si stretching. The bands in 1000 to 1100 cm-1 range are attributed to Si-O-Si stretching vibrations in the inorganic skeleton. The vibrational signals in the range of 800 cm^{-1} in the spectra are also attributed to the bending of Si-O-Si bonds.

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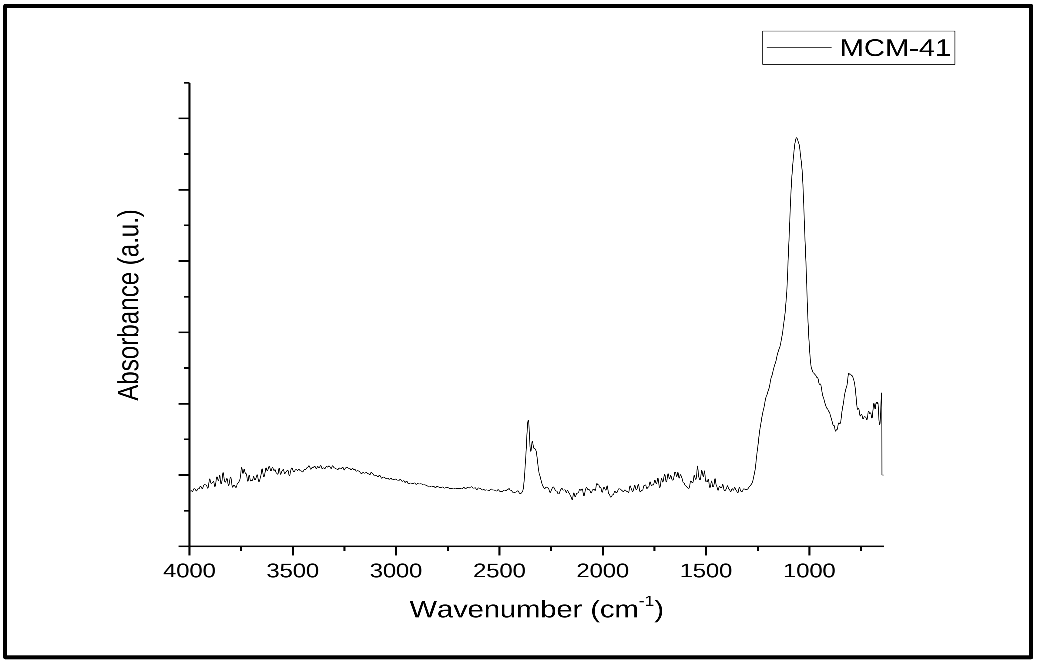

Figure 4.2 FTIR spectra for Mesoporous silica MCM-41

Scanning Electron Microscopy

The surface morphology of Silica material MCM-41 was observed by a scanning electron microscope. Figures 4.3 and 4.4 illustrate the formation of spherical particles observed at two different magnification powers of 5.00 kx and 10.0 kx.

The surface morphology of Silica material MCM-41 was observed by a scanning electron microscope. Figure 4.3 and 4.4 which illustrate the formation of spiracle nanoparticles observed at two different magnification powers of 5.00 kx and 10.0 kx. The nanoparticles of synthesized MCM-41 form small round particles, with an average particle size of approximately 3nm.

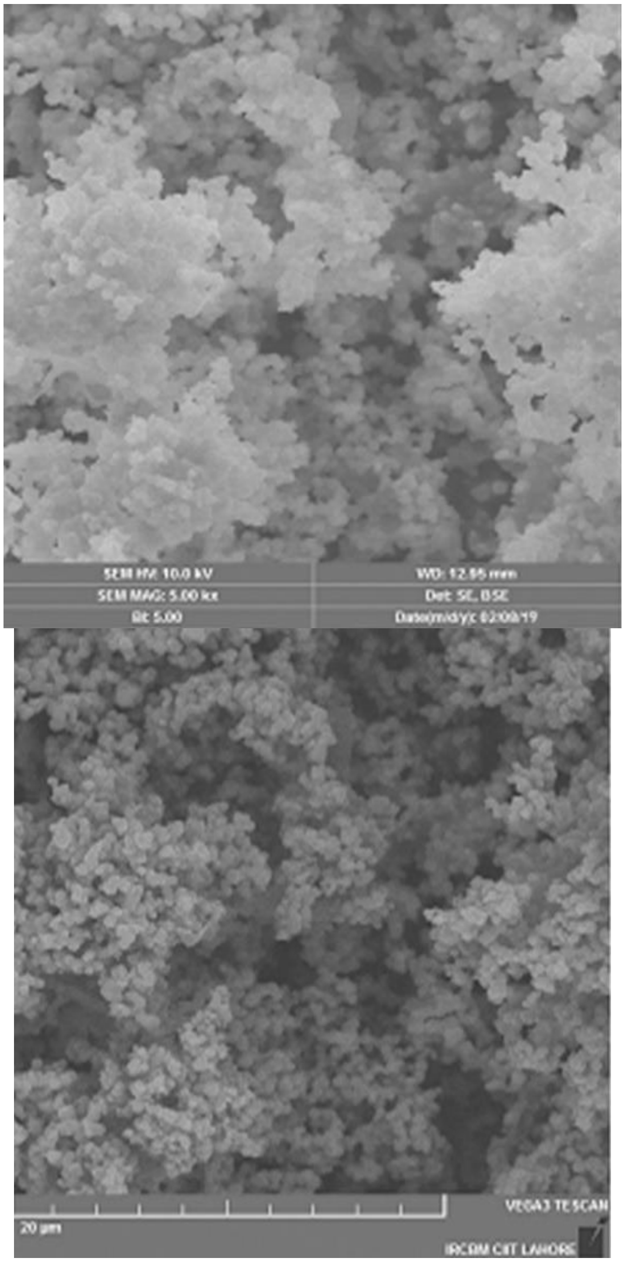

Figure 4.3 Scanning electron micrograph of MCM-41 with a 20 µm scale bar and 5.0 Kx magnification

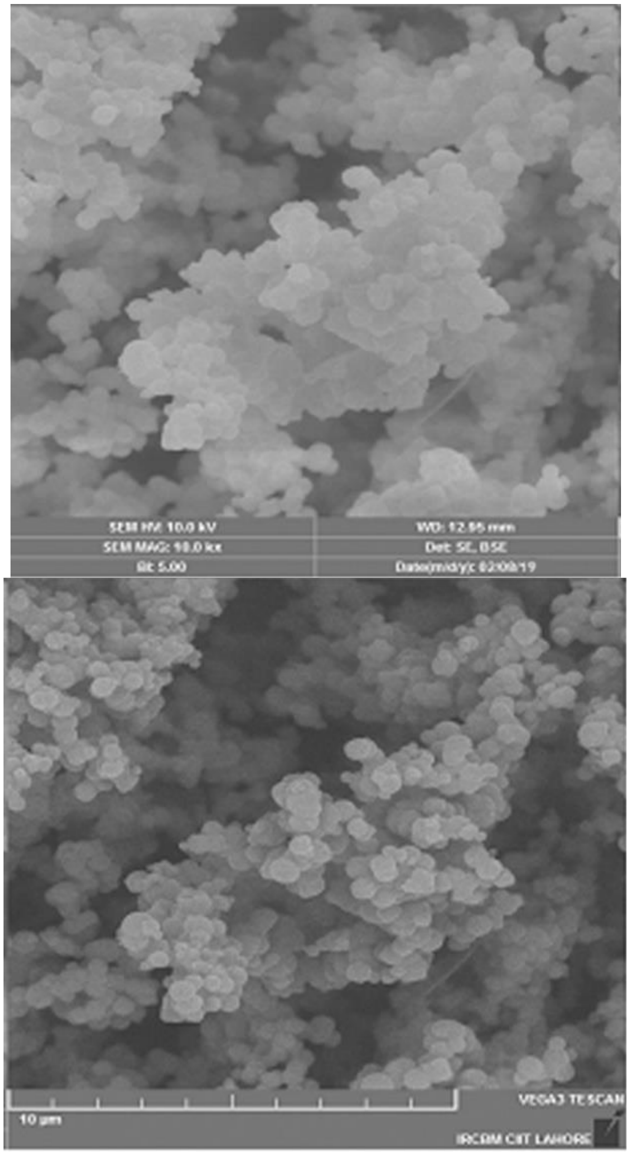

Figure 4.3 "Scanning electron microscopy of mesoporous silica MCM-41 with 10 μm and 10.0Kx magnification".

Drug Encapsulation

The results of the drug loading of ciprofloxacin and declatasvir are shown in figure 4.5 which shows that 38.70% of ciprofloxacin is loaded onto mesoporous silica MCM-41 and 45.52% of declatasvir is loaded on mesoporous silica MCM-41. Declatasvir has a higher loading capacity as compared to ciprofloxacin on mesoporous silica MCM-41.[26].

The procedure of medicine loading was performed by using two-drug i.e., ciprofloxacin and daclatasvir. Mesoporous silica was directly soaked into the drug solutions for 24 hours. Water was used as a drug vehicle for ciprofloxacin and ethanol for declatasvir. After 24 hours the percentage of the loaded drug on the material was decreasing. The percentage of drug loading is summarised in figure 4.5, which shows that 37.80% ciprofloxacin and 45.50% of daclatasvir was loaded on MCM-4. Daclatasvir has more loading capacity as compared to ciprofloxacin The method used in this procedure was based on previously reported studies[27]. The drug loading is influenced by certain parameters including textural properties of a material as well as therapeutic agent, pH, and temperature of loading solution along with the interaction of specific functional groups present in drug structure. [28]

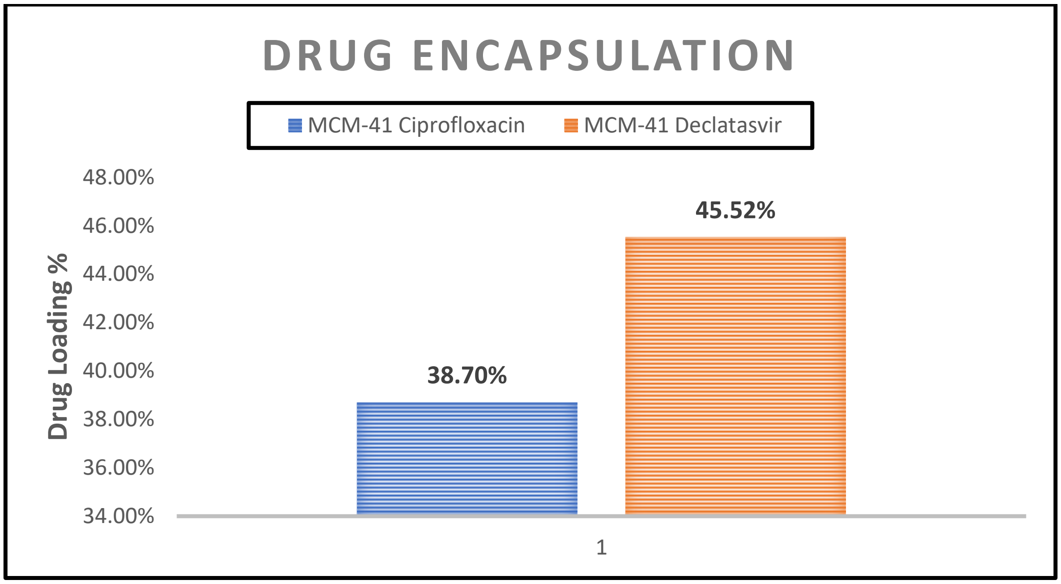

Figure 4.5 Encapsulation of different drugs onto mesoporous silica nanoparticles.

In Vitro Drug Release Studies

The studies on the in-vitro release of ciprofloxacin loaded MCM-41 are given in figure 4.6. which shows the relative release of ciprofloxacin from MCM-41 in HCL and PBS medium. 73.3% of ciprofloxacin is released in the HCL medium while only 32.4% is released in PBS medium in 24 hours. The in-vitro drug release studies of declatasvir loaded MCM-41 is given in figure4.7. which shows the relative release of declatasvir from MCM-41 in HCL and PBS medium. 72.1% of ciprofloxacin is release in PBS medium while only 41.2% is released in HCL medium in 24 hours.

The main driving mechanisms that transfer the drug from the drug carrier to the surrounding medium are often dispersion, thickening of the polymeric matrix, and carrier material degradation.[29]. The release mechanism is divided into three groups based on the physical and chemical properties of the polymer: (i) "diffusion from non-degradation polymer" (ii) "diffusion from polymer swelling; and (iii) "release owing to polymer degradation"[30]

In vitro, the drug release profile for ciprofloxacin and daclatasvir was studied. Type 2 dissolution apparatus was used for the procedure. Phosphate buffered saline PBS a water-based salt solution that is isotonic to the human body and 0.1 M hydrochloride solution (HCL) is used as a dissolution medium. Both the loaded drugs were studied for their maximum release in both mediums. The results of in vitro drug release studies are shown Figures 4.6 and 4.7. It clearly shows that ciprofloxacin loaded MCM-41 releases about 73% of the drug in HCL solution and 32.4% in PBS solution. Daclatasvir loaded MCM-41 releases about 41.2% in HCL solution and 72.1% in PBS solution.[31] The drug release profile was studied for 24 hours. The initial release of ciprofloxacin from McM-41 in HCL medium is 17.8% and in PBS medium the initial release is 11.6%. Both the drug's release profile was compared in their relative medium for 24 hours. By this drug release profile of both drugs loaded mesoporous silica MCM-41 it is shown that the mesoporous silicaMCM-41 can be used as a potential drug carrier. It can also be used in an extended-release drug delivery system.[7, 11]

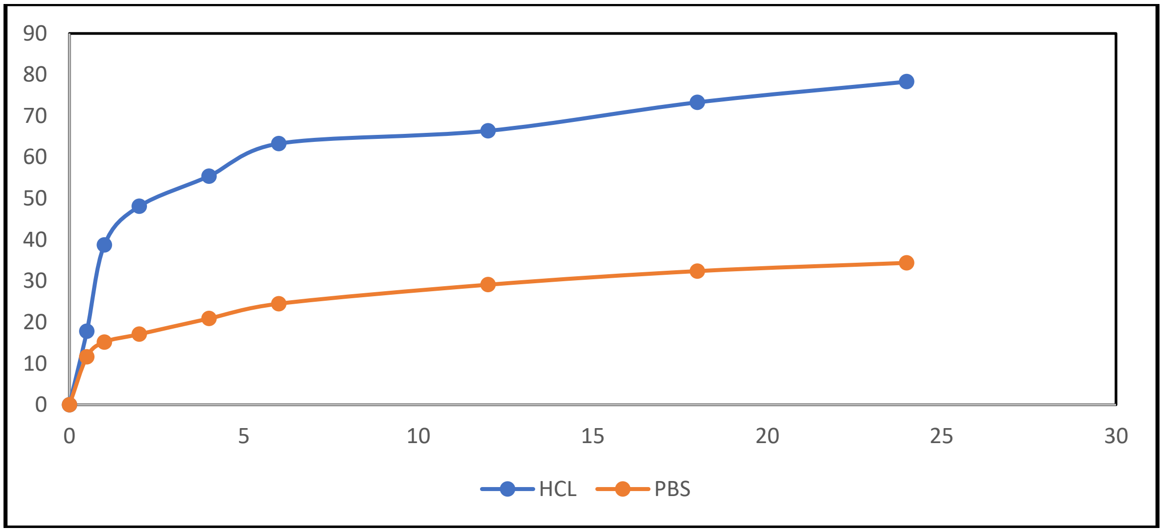

Figure 4.6 In vitro drug release of Ciprofloxacin -MCM-41 into HCL and PBS

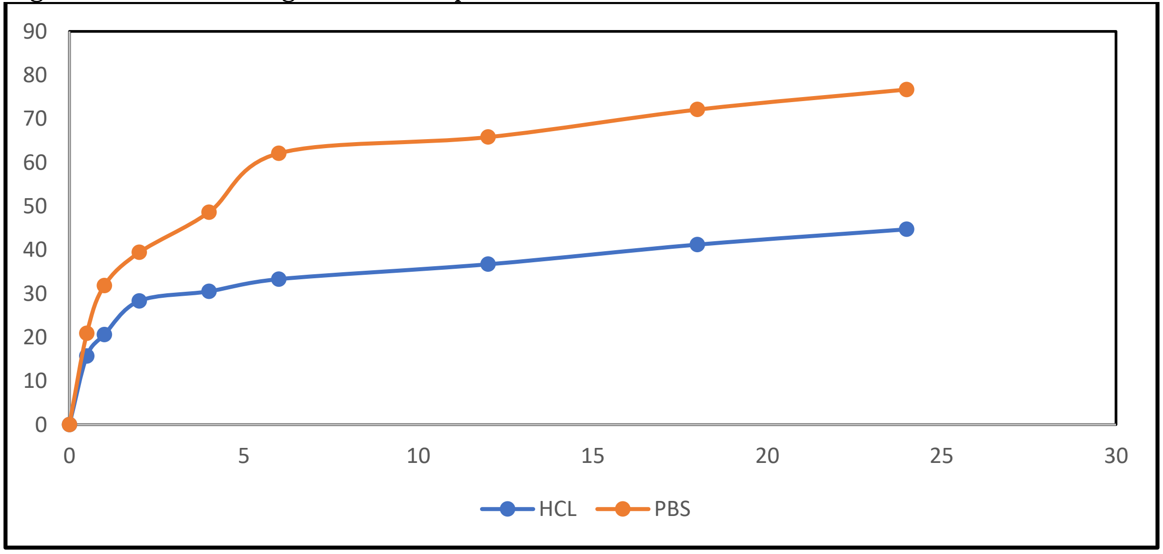

Figure 4.7 In vitro drug release of Daclatasvir-MCM-41 into HCL and PBS

Conclusion:

The drug was successfully loaded on nanoparticles of mesoporous silica. The stable structure and high surface area of MCM-41 results in good drug loading efficiency. MCM-41 is biocompatible which is used by biological systems. "Scanning electron microscopy, infrared spectroscopy, X-ray diffraction analysis, and nitrogen adsorption/ desorption analysis" are used to further characterize the material. The materials medication content was verified using UV visible spectroscopy. The in-vitro drug release experiments provide additional evidence of the drugs bioavailability in comparative solutions. It is possible to draw the conclusion that mesoporous silica is a potential drug carrier and can be employed to deliver various other medications over an extended period.

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