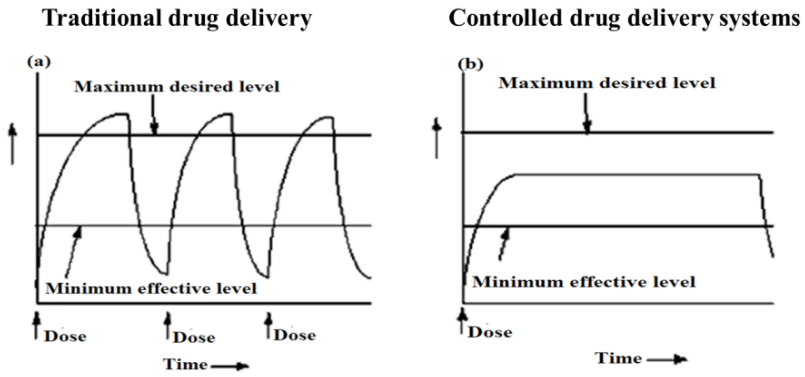
Introduction

Control drug delivery system can be described as formulation that controls the rate and period of drug delivery that is time release doses. Control drug delivery system can deliver precise quantities of therapeutic drugs in tailored release manner to enhance drug efficiency and reduce toxicity. The conventional dosage forms provide drug release immediately and it causes fluctuation of drug level in blood depending upon dosage form.



Scheme 1. Release profile of drug in traditional and controlled drug delivery systems

The drug delivery system should efficiently encapsulate drugs at high concentration and release it in controlled manner for a prescribed period of time.

Hydrogels, Liposomes, polymeric micelles and vesicles are some of the example of drug delivery systems which have been earlier used. However, they have some limitations like Poor chemical stability, rapid elimination by body functioning processes, lack of homogeneous distribution of drug which affects the release rate. Further, specifically designed macroscopic and microscopic structural and chemical features are lacking in polymers.

The ordered mesoporous silica (MCM-41 and MCM-48) is consider as very good drug delivery system because of their typical characteristics, such as highly regular pore structure, uniform pore size and high surface area. The pore size and pore volume can be tailored selectively to bind molecules of various size. There are abundant Si-OH groups on interior and outer surface of materials which can be functionalized for better control over the drug diffusion kinetics [1]. Numbers of reports are available on mesoporous silica functionalized by organic moiety such as Long alkyl chain containing amino group, carboxylic group and thiol group, etc.

So it was a thought of interest to use polyoxometalates, mainly 12-tungstophosphoric acid for functionalisation instead of traditional organic moiety. Polyoxometalates are early transition metal oxygen anion clusters with metal in their higher oxidation state like W (VI), Mo (VI), V(V). They show the property of multifunctionality, structural mobility and easy alteration of chemical composition. Cysteine, L-arginine, Aspirin, Captopril and Camptothecin are selected for the study, because of the following reasons.

Cysteine is a sulfur-based amino acid, cysteine itself can act as an antioxidant in the body, its pro-drugs are used to treat Schizophrenia and reduce drug cravings [2]. It is a limiting substrate in the production of glutathione in the body. Current cysteine therapies are administration of different cysteine derivatives such as N-acetylcysteine. One of the major drawbacks of these therapies is high dosages that can provoke persistent damage and strong allergic reactions [3-6].

L-arginine intravenously administered to the patients with coronary artery disease to increase vascular nitric oxide (NO) bioavailability which show the vasodilatory effect. But the oral administration of arginine does not show this effect. So oral administration of L-arginine via drug delivery system using MCM-41 can overcome this problem and provide L-arginine for NO production[7,8].

A poorly-water soluble drug, aspirin is primarily used for the treatment of cardiovascular diseases1 and as a non-steroidal anti-inflammatory drug which acts by inhibiting the enzyme cyclooxygenase. Captopril is water soluble drug and used in the treatment of controlling blood pressure, heart failure, preventing cardiac remodeling and left ventricular dysfunction after myocardial infection, and preventing kidney damage in human with hypertension and diabetes [9,10]. The elimination half -life of all this drugs is very short which can be overcome using drug delivery system. Camptothecin (CPT) is a naturally occurring quinolone alkaloid which shows significant anticancer activity with a broad spectrum of human malignancies and CPT is an inhibitor of the DNA-replicating enzyme topoisomerase-I [11]. Unfortunately, the clinical application of CPT is hindered by its poor pharmaceutical profile, with extreme aqueous insolubility, low stability of the lactone form at physiological pH, and severe systemic toxicities which included myelosuppression, vomiting, diarrhoea, and hemorrhagic cystitis [12-16].

Therefore, the development of controlled delivery strategies could lead to significant advantages in the clinical use of these drugs.

The objectives have been planned as follows.

- To develop controlled drug delivery system based on mesoporous silica (MCM-41 and MCM-48) and polyoxometalates.
- To synthesize MCM-41 and MCM-48 and characterize them using various techniques such as XRD, SEM, TEM, FTIR, NMR, TG-DTA, BET analysis. \
- To load Cysteine, L-arginine, Aspirin, Captopril as well as Camptothecin into MCM-41 and MCM-48 and characterize them using same techniques.
- To study the in vitro drug release in simulated body fluid (similar to blood plasma pH 7.4) and gastric fluid (pH 1.2). All the processes will be monitored using UV-Visible spectrometry, under stirring and static condition.
- To functionalize MCM-41 and MCM-48 using 12-tungstophosphoricacid (TPA), loading with the mentioned aminoacids/drugs and their characterization.
- To see the effect of functionalization on release profile of drug molecules.
- To study the kinetics and release mechanism of drugs using well known models such as 1st order release kinetic model, Higuchi model, Korsmeyer-Peppas model(KPM) and Extended kinetic model (EKM).
- MTT study for selected drug delivery system.

The thesis is divided into two part.

Part A

Chapter 1 describes synthesis of MCM-41and its functionalization by TPA. Functionalization was carried out by incipient wet impregnation method where, 1 g of MCM-41 was impregnated with 30% aqueous solution of TPA and designated as TPA-MCM-41.

Loading of Cysteine into MCM-41 was carried out by two methods: (a) Soaking and (b) incipient wet impregnation where 15% of cysteine was loaded into MCM-41. The obtained materials were designated as Cys/MCM-41 and Cys/MCM-41(I) for Soaking and incipient wet impregnation method respectively. The amount of drug loading was obtained by analyzing

filtrate by UV-Visible spectrophotometer. 10% of L-arginine was also loaded by incipient wet impregnation method.

In the present release study, materials synthesized by soaking method were found more appropriate for control delivery of cysteine as compare to that of impregnation method.

Here, soaking method was used to load aspirin, Captopril and Camptothecin were also loaded into MCM-41 and TPA-MCM-41. The prepared materials were designated as Asp/MCM-41, Asp/TPA-MCM-41, Cap/MCM-41, Cap/TPA-MCM-41, CPT/MCM-41 and CPT/TPA-MCM-41. The amount of drug loading was obtained by analyzing filtrate at 296 nm, 203 nm, 370 nm by UV-Visible spectrophotometer.

Table 1. Loading amount of drug obtained by UV-Visible spectroscopic analysis

Drugs	Materials			
	% Loading		Amount of drug mg/g of materials	
	MCM-41	TPA-MCM-41	MCM-41	TPA-MCM-41
Aspirin	5.2 ± 2	3.8 ± 2	52 ± 2	38 ± 2
Captopril	5.2 ± 2	4.9 ± 2	52 ± 2	49 ± 2
Camptothecin	7.1 ± 2	4.9 ± 2	71± 2	49 ± 2

Higher drug loading is observed in case of MCM-41 compared to TPA-MCM-41. This may be because the mesoporous channels of MCM-41 are already filled with TPA. So there is lesser space for accommodation of drug molecules.

All the prepared materials were characterized by various physicochemical techniques such as TGA, FTIR, BET surface area analysis, low angle Powder XRD and TEM. For example, the detailed characterization of Aspirin loaded MCM-41 and TPA-MCM-41 are shown here.

Characterizations

The nitrogen adsorption-desorption isotherm and pore size distribution curve for MCM-41, Asp-MCM-41, TPA-MCM-41 and Asp/TPA-MCM-41 are shown in Figure 1, and the textural parameter are shown in Table 2. The isotherm is type (IV) in nature for all the four systems which confirms the formation of mesoporous structure. From Table 1 it can be seen that, Asp-MCM-41, TPA-MCM-41 and Asp/TPA-MCM-41 show significant decrease in BET surface area

and pore volume as compare to MCM-41. This is the first indication for the encapsulation of aspirin in to the pores of mesoporous materials. Decrease in all BET parameters of Asp-MCM-41 and Asp/TPA-MCM-41 suggests the strong interaction between the aspirin and the carriers.

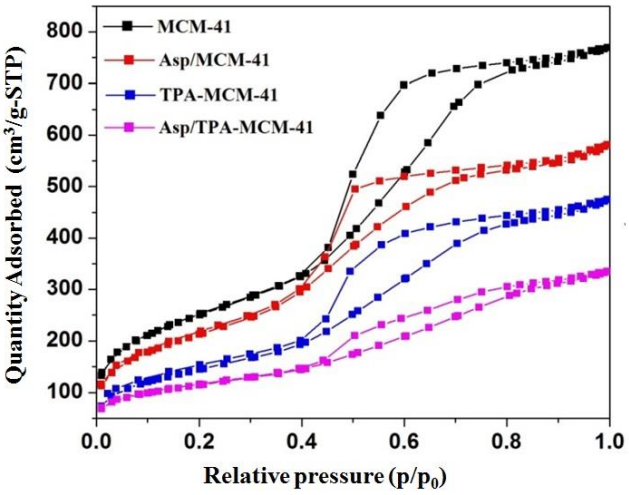


Fig.1. Nitrogen adsorption-desorption isotherm of MCM-41, Asp/MCM-41, TPA-MCM-41 and Asp/TPA-MCM-41

Table 2. Textural property of MCM-41, Asp/MCM-41, TPA-MCM-41 and Asp/TPA-MCM-41

Materials	Specific surface area (m^2/g)	Pore volume (cm^3)/g
MCM-41	890	1.19
Asp-MCM-41	764	0.91
TPA-MCM-41	622	0.71
Asp/TPA-MCM-41	511	0.56

MCM-41 shows FT-IR broad band around 1100–1300 cm^{-1} corresponds to asymmetric stretching vibration of Si–O–Si. The band at 801 and 498 cm^{-1} corresponds to symmetric stretching and bending vibration of Si–O–Si, respectively. The broad band at 3448 cm^{-1} corresponds to symmetric stretching vibration of Si–OH group. Aspirin shows FTIR bands at 1630 cm^{-1}, 3300-3500 cm^{-1},1020-1275 cm^{-1} and 545 cm^{-1} corresponding to C=O stretching vibration, O-H stretching vibration, C-O stretching vibration and CO_2 rocking vibration [17,18] The FTIR bands at 1638 cm^{-1}, 569 cm^{-1} and 966 cm^{-1} are observed in case of Asp-MCM-41

corresponds to C=O stretching vibration, CO_2 rocking vibration and C-O stretching vibration respectively, indicating the presence of aspirin in the carriers. Shifting in bands from 545 cm^{-1} to 569 cm^{-1} as well as from 1020 cm^{-1} to 966 cm^{-1} in case of Asp-MCM-41 suggests the interaction of carbonyl group of aspirin with Si-OH group of carriers.

The low angle XRD pattern of MCM-41(Fig. 2) shows an intense diffraction peak at 2θ = 2° which are assigned to the lattice faces (100), suggesting a hexagonal symmetry of MCM-41 along with the secondary reflection at 2θ = 3-5° with very low intensity. The 2θ peak at 1.9º is observed for Asp-MCM-41 (Fig.2). Shifting in 2θ peak suggests the encapsulation of aspirin into carriers as well as intact structure of carriers. The XRD of TPA-MCM-41 also shows similar pattern of peak at 2θ = 2° with lower intensity which suggest the intact structure of MCM-41 even after functionalization. However, decrease in peak intensity indicates the presence of TPA into MCM-41.

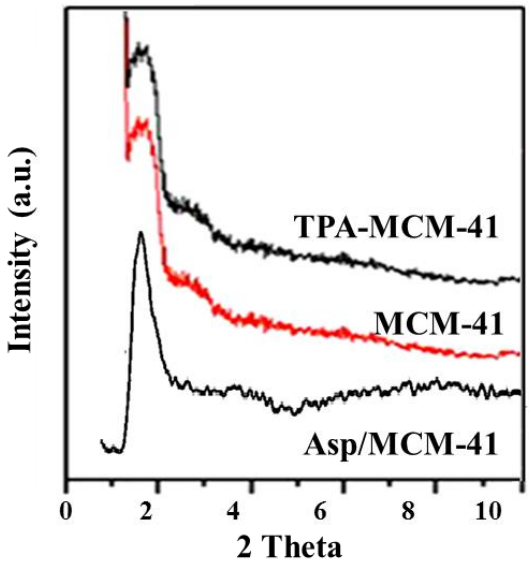
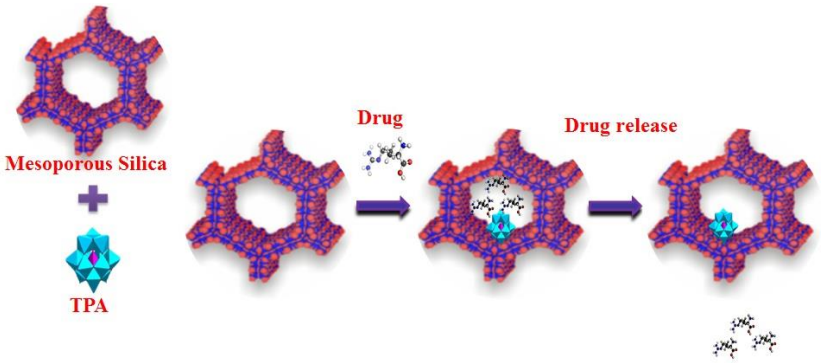


Fig.2. Low angle powder XRD of MCM-41, TPA-MCM-41 and Asp/MCM-41



Scheme 2. Drug release from TPA functionalized mesoporous silica

Chapter 2 describes the in vitro release of drugs (Aspirin, Captopril and Camptothecin) from MCM-41 and TPA-MCM-41. Release profile was obtained by soaking drug loaded materials into simulated body fluid (SBF) under stirring condition at body temperature. At predetermined time interval release fluid was collected and fresh SBF was added to the systems to maintain the constant volume. The amount of aspirin released was obtained by analyzing release fluid at 296 nm using UV-Visible spectrophotometer.

Table 1 shows release data of Aspirin loaded into MCM-41 and TPA-MCM-41. For finding effect of stirring on release rate of drugs, release study was carried out under stirring static condition. Under static condition, slower release rate was observed compared to stirring condition. This is may be the results of slower diffusion of drug molecules from carrier under static condition for both systems (MCM-41 and TPA-MCM-41).

Table 1. Effect of stirring on release rate of Aspirin from MCM-41 and TPA-MCM-41

Condition	**Stirring condition**			**Static condition**		
	Initial	**After 10h**	**30 h**	**Initial**	**After 10h**	**30 h**
Asp/MCM-41	41	61	97	12	15	24
Asp/TPA-MCM-41	25	56	89	10	14	24

To study the drug release kinetics and mechanism, release data up to 10 h are fitted to First order release kinetic model, Higuchi Model, Korsmeyer-Peppas Model (KPM) and Extended Kinetic Model (EKM) and data are shown in Table 2.

First order release kinetic model is used to understand release kinetic of drug from porous matrix like MCM-41 and MCM-48. Higuchi model is used to understand drug release mechanism. According to this model, mechanism of drug release involved simultaneous penetration of surrounding medium, dissolution of drug molecules into the medium and diffusion of drug molecules from the channels of carrier. Korsmeyer-Peppas Model was also used to understand mechanism of drug release. The value of n (diffusion exponent) shows that which mechanism was followed. Extended Kinetic model describes diffusion steps for the drug transport in pores and in the external liquid film (surrounding the support particle) to the receptor body fluid (considered homogeneous).

Kinetic data shows that more ordered release profile was obtained for TPA-MCM-41 system compared to pure MCM-41. Release of drug follows first order release kinetic model and Higuchi model. Value of n (diffusion exponent) suggests the release of Aspirin follow fickian diffusion mechanism. Desorption-adsorption equilibrium constant K (EKM Model) is higher for MCM-41 compared to TPA-MCM-41, which suggests the slower release of drugs from TPA-MCM-41.

Table 2. Kinetic and mechanistic parameter of Aspirin release from MCM-41 and TPA-MCM-41

Materials	First order release kinetic Model	Higuchi Model	Korsmeyer-Peppas Model	Extended Kinetic Model
Asp/MCM-41	0.9545	0.979	0.964 n= 0.47	K = 5.60
Asp/TPA-MCM-41	0.9514	0.9894	0.9739 n=0.49	K = 4.59

For finding effect of TPA on release rate release data of drug loaded into pure MCM-41 and TPA-MCM-41 were compared and data are shown in Table 3. In case of Asp/TPA-MCM-41, initially only 25% of aspirin was release and reached to 56% up to 10, while in case of Asp/MCM-41, 41% of drug was released and reached to 56% up to 10 h. Slower release rate for Asp/TPA-MCM-41 compared to asp/MCM-41, is may be due to the strong interaction of Aspirin molecules with TPA-MCM-41.

Table 3. In vitro release profile of Aspirin from MCM-41 and TPA-MCM-41

Materials	% of Drug release		
	Initial	After 10h	30 h
Asp/MCM-41	41	61	97
Asp/TPA-MCM-41	25	56	89

Similar in vitro release study was also carried out for rest of the drugs which also support that functionalization of MCM-41 by TPA decrease the release rate of drug. Further, the kinetic study also shows that release of drugs follow first order release kinetic model and fickian diffusion mechanism.

MTT study of MCM-41, TPA-MCM-41, CPT/MCM-41, CPT/TPA-MCM-41 and pure CPT was carried out using HePG2 cancer cells. MCM-41 showed ≤ 10% cytotoxicity in the said doses (0.1, 0.3, 0.5 mg/ml, Fig. 6). The functionalized material, TPA-MCM-41 recorded < 30% cytotoxicity whereas functionalized carrier loaded with drug CPT (CPT/TPA-MCM-41) showed > 40% at 0.5 mg/ml dose. These observations are of relevance because CPT/TPA-MCM-41 (at 0.5 mg/ml) accounted for 9.2% higher cytotoxicity than CPT treated group at the same dose. Overall, the results indicate that the TPA-MCM-41 carrier is non-toxic to the cells but the drug loaded carrier accounts for highest percentage of cytotoxicity amongst all groups. These results imply towards CPT/TPA-MCM-41 mediated improved delivery of CPT that can be of significance in cancer therapy.

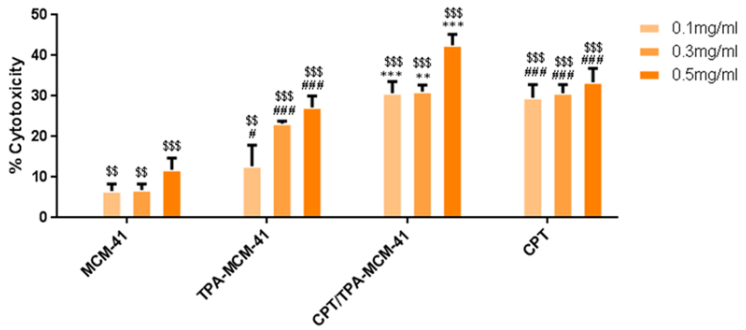


Fig.1 Effect of materials on the cytotoxicity of HepG2 cells

Chapter 3 describes the in vitro release and kinetic study of amino acids from MCM-41. Release profile was obtained by same method as stated earlier. The amount of amino acid released was

obtained by treating it with 10% ninhydrin solution in ethanol at 570 nm using UV-Visible spectrophotometer.

Table 1. Shows release profile of Cys/MCM-41(I) and Cys/MCM-41. Slower release profile was obtained for the material which is prepared by soaking method compared to one which is prepared by incipient wet impregnation method. This is may be due the higher concentration of cysteine molecules on the outer surface of MCM-41 (for Cys/MCM-41(I)) prepared by impregnation method.

Table 1. In vitro release profile of Cys/MCM-41(I) and Cys/MCM-41

Materials	**% of Drug release**		
	Initial	**After 10h**	**30 h**
(a) Cys-MCM-41(I)	**60**	**82**	**98**
(b) Cys-MCM-41	**38**	**70**	**91**

Further to see the effect of stirring, in vitro release study was carried out under stirring and static condition. Table 2. Shows release profile of Cysteine under stirring and static condition. Under static condition, slower release was observed which may be due to the slower diffusion of cysteine from MCM-41.

Table 2. Effect of stirring on release rate of cysteine

Condition	**% of Cysteine release**		
	Initial	**After 10h**	**30 h**
(a) Stirring	38	70	91
(b) Static	30	51	80

To investigate kinetics and mechanism of amino acids release first order release kinetic model and Higuchi model were applied. Table 3 shows kinetics parameter of Cys/MCM-41(I) and Cys/MCM-41. Kinetic data shows that more ordered release data was obtained for Cys/MCM-41 with higher value of R^2 compared to Cys/MCM-41(I). These suggest that release of Cysteine as well as L-arginine follows first order release kinetic model and Higuchi model.

Table 3. Kinetic and mechanistic parameter of Amino acid release from MCM-41

Materials	First order release kinetic model	Higuchi model
Cys/MCM-41(I)	0.9361	0.963
Cys/MCM-41	0.9864	9955

Similar release and kinetic study was carried out for L-arg/MCM-41.

Part B

Chapter 4 describes synthesis of MCM-48 and its functionalization using TPA by same method as stated earlier. The synthesized materials (MCM-48 and TPA-MCM-48) were characterized by various physicochemical techniques such as TGA, FTIR, BET surface area, low angle powder XRD and TEM. Loading of amino acid/drugs into MCM-48 and TPA-MCM-48 were also carried out by same method as describe earlier and characterized by the same techniques. The synthesized materials were designated as Cys/MCM-48 (I), Cys/MCM-48, L-arg/MCM-48, Asp/MCM-48, Asp/TPA-MCM-48, Cap/MCM-48, Cap/TPA-MCM-48, CPT/MCM-48 and CPT/TPA-MCM-48.

Characterization techniques shows that functionalization of MCM-48 by TPA does not change the structure of MCM-48. It also shows that TPA interacts with MCM-48 through its Si-OH group. Characterization of amino acids/drugs loaded materials shows that they interact with MCM-48 through its Si-OH group and with TPA-MCM-48 through its terminal oxygen. BET surface area analysis suggests the presence of amino acid/drugs into the channels of MCM48 and TPA-MCM-48.

Table 1 shows amount of drug loading into MCM-48 and TPA-MCM-48 in mg/g of materials. Higher drug loading is observed in case of MCM-48 compared to TPA-MCM-48. This is because; mesoporous channels of MCM-48 are already filled with TPA. So there is lesser space for accommodation of drug molecules.

Table 1. Loading amount of drug obtained by UV-Visible spectroscopic analysis

Drugs	Materials			
	% Loading		Amount of drug mg/g of materials	
	MCM-48	TPA-MCM-48	MCM-48	TPA-MCM-48
Aspirin	4.8 ± 2	3.6 ± 2	48 ± 2	36 ± 2
Captopril	5.5 ± 2	4.5 ± 2	52 ± 2	45 ± 2
Camptothecin	8 ± 2	7.5 ± 2	80 ± 2	75 ± 2

Chapter 5 describes the in vitro release of drugs (Aspirin, Captopril and Camptothecin) from MCM-48 and TPA-MCM-48 which was obtained by same method as stated earlier. Table 1 shows release data of Aspirin loaded into MCM-48 and TPA-MCM-48 under stirring and static condition. Under static condition, slower release rate was observed compared to stirring condition. This is may be the results of slower diffusion of drug molecules from carrier under static condition.

Table 1. Effect of stirring on release rate of drugs from MCM-48 and TPA-MCM-48

Condition	Stirring condition			Static condition		
	Initial	After 10h	30 h	Initial	After 10h	30 h
Asp/MCM-48	43	80	97	12	19	24
Asp/TPA-MCM-48	38	71	81	10	19	25

To study the drug release kinetics and mechanism, release data up to 10 h are fitted to First order release kinetic model, Higuchi Model, Korsmeyer-Peppas Model (KPM) and Extended Kinetic Model (EKM) and data are shown in Table 2.

Kinetic data shows that more ordered release profile was obtained for TPA-MCM-48 system compared to pure MCM-48. Release of drug follows first order release kinetic model and Higuchi model. Value of n (diffusion exponent) suggests the release of Aspirin follow fickian diffusion mechanism. Desorption-adsorption equilibrium constant K (EKM Model) is higher for MCM-48 compared to TPA-MCM-48, which suggests the slower release of drugs from TPA-MCM-48.

Table 2. Kinetic and mechanistic parameter of Aspirin release from MCM-48 and TPA-MCM-48

Materials	First order release kinetic Model	Higuchi Model	Korsmeyer-Peppas Model	Extended Kinetic model
Asp/MCM-48	0.964	0.970	0.953 n = 0.48	$K = 9.0* 10^{-2}$
Asp/TPA-MCM-48	0.925	0.969	0.995 n = 0.5	$K = 6.3* 10^{-2}$

For finding effect of TPA on release rate release data of drug loaded into pure MCM-48 and TPA-MCM-48 were compared. In case of Asp/TPA-MCM-48, initially only 38% of aspirin was release and reached to 71% up to 10, while in case of Asp/MCM-48, 43% of drug was released and reached to 80% up to 10 h. Slower release rate for Asp/TPA-MCM-48 compared to asp/MCM-48, is may be due to the strong interaction of Aspirin molecules with TPA-MCM-48.

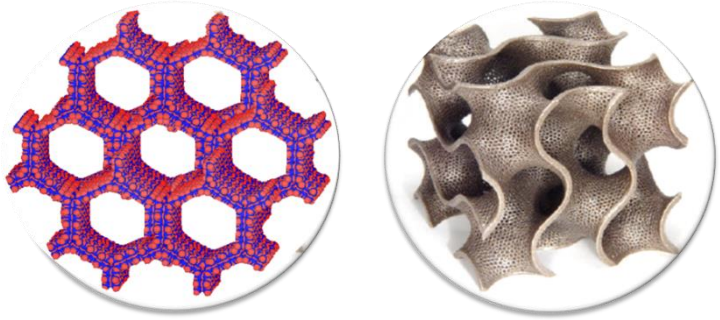
Table 3. In vitro release profile of Aspirin from MCM-48 and TPA-MCM-48

Materials	% of Drug release		
	Initial	**After 10h**	**30 h**
Asp/MCM-48	43	80	97
Asp/TPA-MCM-48	38	71	81

Similar in vitro release study was also carried out for rest of the drugs which also support that functionalization of MCM-48 by TPA decrease the release rate of drug. Further, the kinetic study also shows that release of drugs follow first order release kinetic model and fickian diffusion mechanism.

To see the effect of carrier release profile of drugs loaded into MCM-41 and MCM-48 as well as TPA-MCM-41 and TPA-MCM-48 were compared and results are shown in table 4. It is well known that the pore size as well as the geometry of carrier has a pronounced influence on the kinetics of drug release. In present case, MCM-48 shows faster release of drug molecules compared to MCM-41 as 3D interconnected pore System of MCM-48 allow well-massed

transportation compared to MCM-41 which is having 2D channels. The same release trend was observed for all systems.



Scheme 3. Structure of MCM-41(left) and MCM-48 (Right)

Table 4. Effect of carrier on release rate of drugs

Materials	% of Drug release			Materials	% of Drug release		
	Initial	After 10h	30 h		Initial	After 10h	30 h
Asp/MCM-41	41	61	97	**Asp/TPA-MCM-41**	25	56	89
Asp/MCM-48	43	80	97	**Asp/TPA-MCM-48**	38	71	81
Cap/MCM-41	44	83	96	**Cap/TPA-MCM-41**	34	67	89
Cap/MCM-48	46	94	98	**Cap/TPA-MCM-48**	33	65	93
CPT/MCM-41	28	72	98	**CPT/TPA-MCM-41**	21	62	90
CPT/MCM-48	36	74	98	**CPT/TPA-MCM-48**	30	68	97

Chapter 6 describes the in vitro release and kinetic study of amino acids from MCM-48. Table 1. Shows release profile of Cys/MCM-48(I) and Cys/MCM-48. Slower release profile was obtained for the material which is prepared by soaking method compared to one which is prepared by incipient wet impregnation method. This is may be due the higher concentration of cysteine molecules on the outer surface of MCM-48 (for Cys/MCM-48(I)) prepared by impregnation method. Further, release study was carried out under static condition and data are compared. Slower release was observed under static condition which may be due to the slower diffusion of cysteine from MCM-48.

Table 1. In vitro release profile of (a) Cys/MCM-48(I), (b) Cys/MCM-48 (stirring condition) and (c) under static condition

Materials	% of Drug release		
	Initial	After 10h	30 h
(a) Cys-MCM-48(I)	51	85	98
(b) Cys-MCM-48 (Stirring condition)	34	76	91
(c) Cys-MCM-48 (Static condition)	28	49	70

To investigate kinetics and mechanism of amino acids release first order release kinetic model and Higuchi model were applied to release data. Table 2 shows kinetics parameter of Cys/MCM-48(I) and Cys/MCM-48. Kinetic data shows that more ordered release data was obtained for Cys/MCM-48 with higher value of R^2 compared to Cys/MCM-48(I). These suggest that release of Cysteine follows First order release kinetic model and Higuchi model.

Table 2. Kinetic and mechanistic parameter of Amino acid release from MCM-48

Materials	First order release kinetic model	Higuchi model
Cys/MCM-48(I)	0.9565	0.977
Cys/MCM-48	0.9948	0.991
Cys/MCM-48	0.9948	0.991

Similar in vitro release and kinetic study was also carried out for L-arg/MCM-48.

To see the effect of particle size on drug adsorption as well as on release rate of drug, MCM-41 type mesoporous silica nanoparticle (Np-MCM-41) was synthesized and used as carrier to deliver L-arginine, aspirin and Captopril. All the synthesized materials were well characterized by same techniques. Loading as well as release profile of L-arginine, aspirin and Captopril were obtained by same method as stated earlier.

Table 3 shows amount of drug loading into MCM-41 and Np-MCM-41. Higher loading efficiency for Np-MCM-41 was observed as compared to MCM-41. As Np-MCM-41 has higher specific surface area as compared to MCM-41 and hence has higher adsorption capacity. However, the release profile obtained from Np-MCM-41 was similar to that which was obtained from MCM-41.

Table 3. Comparison of loading efficiency of MCM-41 and Np-MCM-41

Materials	**Surface area (m2/g)**	**Pore Volume (cm3/g)**	**Pore diameter (A^o)**	**Amount of Aspirin mg/g of materials**	**Amount of Captopril mg/g of materials**
MCM-41	890	1.19	49	52 ± 2	52 ± 2
Np-MCM-41	1100	1.06	37	58± 2	67 ± 2

Summary

Controlled drug delivery systems based on functionalized (TPA as anchoring agent) and unfunctionalized mesoporous silica (MCM-41 and MCM-48) were developed and studied for in vitro release of amino acid/Drugs. The synthesized materials were characterized by various physicochemical techniques. The MTT study shows that MCM-41 and TPA-MCM-41 are non-toxic. However, CPT/MCM-41 and CPT/TPA-MCM-41 show toxicity towards the HepG2 cell which is as expected. Release studies shows that more ordered and controlled release of amino acid/drugs were obtained for TPA-MCM-41/TPA-MCM-48 as compared to pure MCM-41/MCM-48. MCM-48 comes out to be better carrier as compared to MCM-41 as due to three dimensional pore network and easy mass transport as well as diffusion properties. Kineticand mechanistic studies shows that release of amino acids/drugs follows first order release kinetic model and fickian diffusion mechanism. Np-MCM-41 also shows better carrier for amino acid/drugs with higher loading capacity compared to MCM-41.

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