Asian Journal of Chemistry; Vol. 25, No. 17 (2013), 9511-9513

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2013.15051

Controlled Release of Ampicillin by Surface Modified MCM-48 Molecular Sieves

BIPUL KUMAR NATH[1,*] and JATINDRA NATH GANGULI[2]

[1]Department of Chemistry, Bilasipara College, Bilasipara-783 348, India
[2]Department of Chemistry, Gauhati University, Guwahati-781 014, India

*Corresponding author: E-mail: nathbipul@yahoo.co.in

(*Received*: 27 December 2012; *Accepted*: 1 October 2013) AJC-14216

The mesoporous MCM-48 molecular sieves was prepared by hydrothermal process and the outside surface of the catalyst was modified with hexamethyldisilazine. Ampicillin is a β-lactam antibiotic drug that has been used extensively to treat bacterial infections since 1961. The drug was doped inside the pores of surface modified catalyst and the drug release was studied from the matrix into a simulated body fluid. The materials were characterized by XRD, FT-IR, SEM and TGA. The drug adsorbed benign MCM-48 may be used for effective drug delivery.

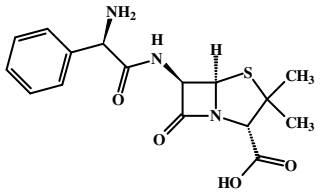
Key Words: Mesoporous, MCM-48, Ampicillin.

INTRODUCTION

The rapidly increasing number of publications about the synthesis, modification and characterization of MCM-48 reflects the growing interest in these mesoporous silica amongst scientist and technologists[1,2]. These mesoporous materials discovered in 1992 by Mobile Researchers[3] were designated as M 41S. The three groups of M 41S are (a) Hexagonal MCM-41 with one-dimensional pores (b) Cubic MCM-48 with three dimensional pores and (c) Lamellar MCM-50. The variable pore sizes (2.0-4.5 nm), high surface area (900-1300 $m^2 g^{-1}$)[4] and possible local structure modification makes these mesoporous material attractive to study adsorption, separation, ion exchange, catalysis and as host structure for nano materials. It has been reported[5] that post treatment can increase its thermal stability. The three dimensional pores of MCM-48 allows faster diffusion of molecules through the channel and unlike MCM-41 makes it more resistant towards pore blocking.

Drug delivery is the process of administering a pharmaceutical compound to achieve a therapeutic effect in human or animals. Drug delivery technologies are patent protected formulation technologies that modify drug release profile, absorption, distribution and elimination, for the benefit of improving product efficacy and safety, as well as patient convenience and compliance. Most common routes of administration include the preferred non-invasive peroral (through the mouth), topical (skin), transmucosal and inhalation routes. Many medicine such as peptide and protein, antibody, vaccine and gene based drugs, in general may not be delivered using these routes because they might be susceptible to enzymatic degradation or can not be absorbed into the systemic circulation efficiently due to molecular size and charges, to be therapeutically effective. Current efforts in the area of drug delivery include the development of targeted delivery in which the drug is only active in the target area of the body and sustained release formulations in which the drug is released over a period of time in a controlled manner from a formulation. Types of sustained release formulations include liposomes, drug loaded biodegradable microspheres and drug polymer conjugates.

Ampicillin is a penicillin β-lactam antibiotic drug that has been used extensively to treat bacterial infections[6] since 1961. Until the introduction of ampicillin by the British company Beecham, penicillin therapies had only been effective against gram-positive organisms such as *staphylococci* and *streptococci*. Ampicillin is a broad spectrum antibiotic active against gram-positive and gram-negative bacteria. This drug is used to kill bacteria, treat a variety of infections such as food poisoning, ear infections, pneumonia, tonsillitis, strep throat, bronchitis, gonorrhea or urinary tract infections. Ampicillins inhibit one of the enzymes involved in the synthesis of the bacterial cell walls. The loss of the stability conferred by the wall leads to the cell lysing. Molecular formula of ampicillin is $C_{16}H_{19}N_3O_4S{\cdot}3H_2O$, having molecular weight 403.5 g and melting point: 313 K. It is white crystalline powder and readily soluble in dilute HCl. It is marketed usually as the sodium salt. The chemical structure of ampicillin is shown below-



6-[[(2R)-Aminophenylacetyl] amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid

In this work we have reported the synthesis of MCM-48, its surface modification, ampicillin loading and its release in simulated body fluid.

EXPERIMENTAL

The materials used were tetraethylorthosilicate (TEOS) (Merck), N-cetyl-N,N,N-trimethylammoniumbromide (CTAB) (Merck), ammonium hydroxide (Merck), ethanol (Merck). Hexamethyldisillazane (HDMS) (Merck), sodium chloride (Merck), potassium chloride (Merck), sodium bicarbonate (Qualigen), calcium chloride (Merck), hydrochloric acid (Merck), trisbuffer $(CH_2OH)_3CNH_2$ (SRL), $MgCl_2{\cdot}6H_2O$ (Merck), Na_2SO_4 (Merck), $K_2HPO_4{\cdot}3H_2O$ (Merck), Ampicillin locally procured from market.

The IR spectra of the compounds were taken in KBr pellet with a Perkin Elmer RXIFT-IR instrument. The XRD of the powdered samples were recorded between 1-10º 2θ values in a powder diffractometer with CuK_α radiation at IISc, [40 kV, 60 mA] using a Rigaku instrument at 0.02º step size and 1 s step time. The SEM image of the samples were recorded with a LEO (Carl Zeiss) Microscope at IIT Guwahati. The surface area of the catalyst was determined with Micromeritics-Tristar-3000 instrument after degassing the sample at 373 K for 1 h and then degassing at 523 K for 3 h. The release pattern of ampicillin drug was studied with the help of UV spectrometry.

Hydrothermal synthesis of MCM-48: The synthesis of MCM-48 was done by literature procedure[7-9]. One part of the product was calcined at 823 K for 6 h by initial slow heating at 5 K per minute in a programmable Muffle furnace (LAB TECH).

Modification of outside surface of MCM-48 molecular sieves: The outside hydroxyl of the surface of MCM-48 was encapped by reaction with HDMS[10]. About 0.5 g of calcined MCM-48 was mixed with a mixture of 10 mL of HDMS and 5 mL of ethanol at room temperature and stirred for 24 h. The solid product was filtered and washed with absolute ethanol and dried at room temperature[11].

RESULTS AND DISCUSSION

IR Study: The IR spectra of the MCM-48 samples (Fig. 1) shows stretching vibration of silanol -OH at 3445 cm^{-1} and the bending vibration of H_2O at 1591 cm^{-1}, the asymmetric and symmetric vibrations of Si-O at 1084 and 795 cm^{-1}, respectively. The sample shows additional bands due to C-H stretching and bending at 2910 and 1452 cm^{-1}, respectively from the template. The bands at 1229 cm^{-1} is due to -Si-O-Si- asymmetric stretching and the bands at 463 cm^{-1} is due to -Si-O-Si- bending and also the bands at 1500-1400 cm^{-1} is due to C-H bending of surfactant hydrocarbon[12,13].

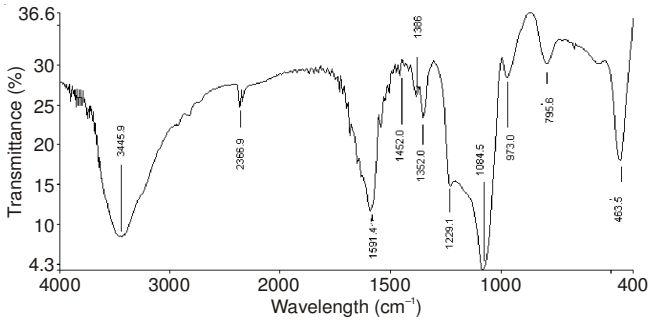


Fig. 1. IR spectra of the MCM-48

XRD studies: The XRD plot of MCM-48 samples shows the characteristic peak at d = 39.14Å (211 plane), d = 23.8 Å (400 plane), 20.6Å (420 plane), 19.02 Å (332 plane) and 18.8 Å (422 plane) consistant with literature values[14]. The characteristic d_{220} peak of MCM-48 was obtained at 32.07 Å in the sample. The XRD plot of drug loaded surface modified MCM-48 samples also shows (Fig. 2) the characteristic d_{220} reflection.

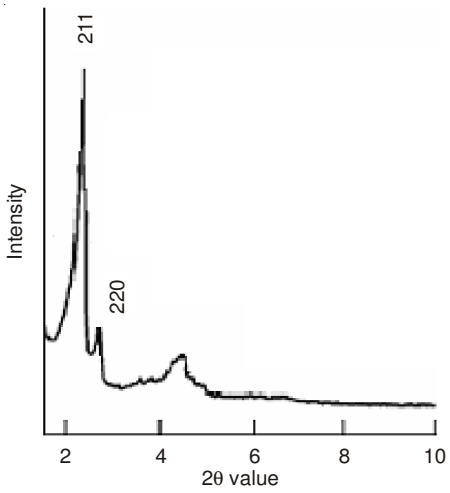


Fig. 2. XRD of drug loaded surface

Scanning electron micrograph (SEM): The SEM image shows (Fig. 3) that the particles were free standing with some aggregation. The particles were varied shape of size 660-840 nm. A close look reveals the unique crystalline morphology.

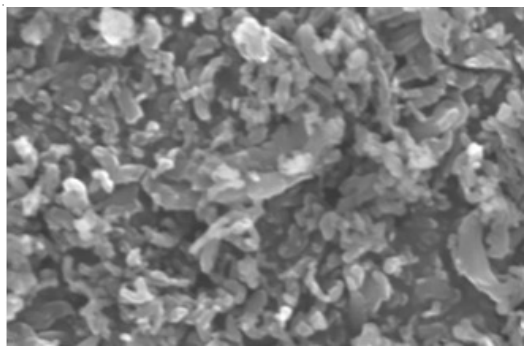


Fig. 3. SEM images of MCM-48 modified MCM-48

Nitrogen adsorption/desorption isotherm: The nitrogen adsorption isotherm shows the type IV isotherm of mesoporous

solid with the hysteresis loop of the MCM-48[15]. Table-1 shows the comparison of the surface area of the carrier.

TABLE-1
SURFACE AREA OF MCM-48

Compounds	Pore volume (cm^3/g)	Pore diameter (nm)	BET surface area (m^2/g)
MCM-48	0.63	2.5	647
SA Modified MCM-48	0.61	2.45	640
Drug loaded SA modified MCM-48	0.25	1.5	452
Drug loaded unmodified MCM-48	0.20	1.35	437

Loading of ampicillin: About 0.2 g of calcined modified MCM-48 was stirred for 24 h at room temperature into 50 mL of ampicillin solution (30 mg/mL HCl). The solid products were filtered, washed with ethanol and dried at room temperature. Similarly loading of ampicillin were also done in calcined unmodified MCM-48. After loading, the surface area, pore volume and pore size decreases which indicate that the drug was loaded in the mesoporous materials. The amount of ampicillin loaded was determined by UV spectroscopy[16] and TG analysis (Fig. 4) and found to be 31 and 24 % in modified and unmodified samples, respectively. The results were consisted with gravimetric analysis of the samples before and after loading.

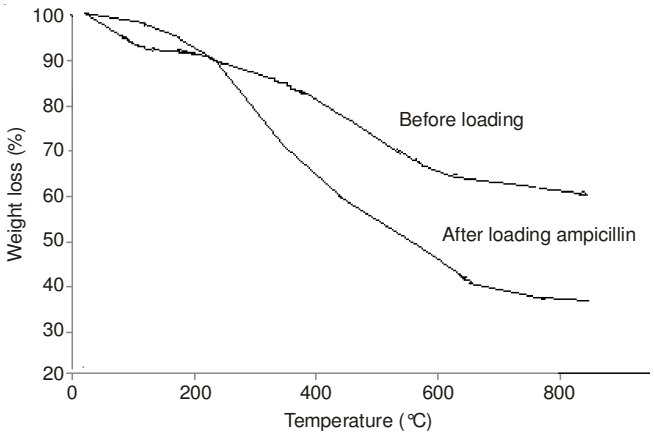


Fig. 4. TGA of the sample before and after loading ampicillin

Preparation of simulated body fluid (SBF): The simulated body fluid which has ion concentrations nearly equal to those of human blood plasma and was buffered at pH 7.40 with 50 mM of trishydroxymethylaminomethane and 45 mM hydrochloric acid at 309 K. The reagents used for preparing simulated body fluid were taken as per literature method[17-19].

Release of ampicillin: The ampicillin loaded MCM-48 were stirred in 50 mL of simulated body fluid at 310 K at pH = 7.40. The amount of ampicillin release were monitored by recording the UV spectra at 324 nm from time to time and the concentration was determined with the help of calibration curve[17]. The release medium was withdrawn at the definite time intervals and replaced with fresh simulated body fluid each time. Then drug release was plotted against time (Fig. 5).

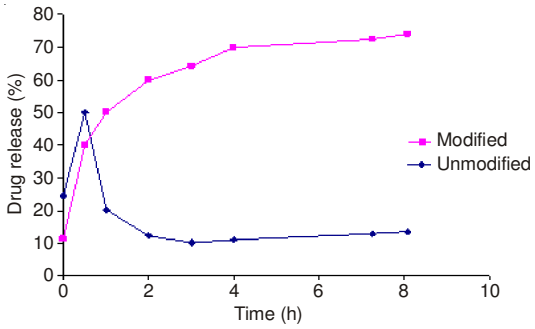


Fig. 5. Ampicillin release profile

50 % of the drug was released by modified MCM-48 within 1.5 h, while rests of the adsorbed drugs were released slowly over a time period of 9 h. This may be because physisorbed drugs were released fast but chemisorbed drugs requires time for release. 75 % of the drug release requires 9 h, which may be because of slow diffusion of the drug from the MCM. In unmodified carrier the drug was adsorbed mostly in outside surface physically and 50 % of the drug was released rapidly in 1 h. After that slow release takes place which may be due to chemically adsorbed drugs inside the pores.

Conclusion

The surface area modified MCM-48 was found to be good carrier for ampicillin. The drug molecules may be controlled released in normal temperature. Therefore MCM-48 may be used for controlled drug release.

ACKNOWLEDGEMENTS

The authors are grateful to CIF-IIT Guwahati; IISc-Bangalore, SAIF-Shillong and Guwahati University for allowing to record different analysis.

REFERENCES

1. T.R.Gaydhankar, U.S.Taralkar,R.K.Jha,P.N.Joshi and R.Kumar, *Catal. Commun.*, **6**, 361 (2005).
2. K. Vidya, N.N. Gupta and P. Selvam, *Mater. Res. Bull.*, **39**, 2035 (2004).
3. C.T. Kresge, M.E. Leonowicz,W.J. Roth, J.C. Vartuli and J.S. Beck, *Nature*, **359**, 710 (1992).
4. S. Gomez, O. Giraldo, L.J. Garces, J. Villegas and S.L. Suib, *Chem. Mater.*, **16**, 2441 (2004).
5. J.H. Sun and M. Coppens, *J. Mater, Chem.*, **12**, 3016 (2002).
6. B. Kasten and R. Reski, *J. Plant Physiol.*, **150**, 137 (1997).
7. S. Gontier and A. Tuel, *J. Catal.*, **157**, 124 (1996).
8. G. Oye, J. Sjobloom and M. Stocker, *J. Disper. Sci. Technol.*, **21**, 49 (2000).
9. B.K. Nath and J.N. Ganguli, *Asian J. Chem.*, **24**, 5292 (2012).
10. J. Jong, M.S. Sarkar, V.B. Takale and S.E. Park, *Bull. Korean Chem. Soc.*, **26**, 1671 (2005).
11. H. Yu and Q.Z. Zahi, *Micropor. Mesopor. Mater.*, **123**, 298 (2009).
12. Q. Peng, Y. Yang and Y. Yuan, *J. Mol. Catal. A*, **219**, 175 (2004).
13. A. Corma, *Chem. Rev.*, **97**, 2407 (1997).
14. B.K. Nath and J.N. Ganguli, *Bull. Catal. Soc. India*, **9**, 121 (2010).
15. B.K. Nath and J.N. Ganguli, *Global Res. Method. J.*, **2**, 7th Issue (2012-13).
16. Y. Zhu, S. Kaskel, T. Ikoma and N. Hanagata, *Micropor. Mesopor. Mater.*, **123**, 107 (2009).
17. T. Kokubo, H. Kushitani, S. Sakka, T. Kitsugi and T. Yamamuro, *J. Biomed. Mater. Res.*, **24**, 721 (1990).
18. C. Ohtsuki, H. Kushitani, T. Kokubo, S. Kotani and T. Yamamuro, *J. Biomed. Mater. Res.*, **25**, 1363 (1991).
19. Y. Zhang and M. Zhang, *J. Biomed. Mater. Res.*, **62**, 378 (2002).