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Original Article

DENSIO-VISCOMETRIC STUDIES OF TIO_2-MCM-41 IN ETHANOLIC NICOTINAMIDE SOLUTIONS AND ITS APPLICATION IN DRUG DELIVERY OF IBUPROFEN

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ABSTRACT

Objective: To study the density, viscosity of the solutions of TiO_2-MCM-41 in the presence of nicotinamide as hydrotropic agent in ethanol solvent at different temperatures ranging from 298.15K to 313.15K at an interval of 5K, and its application as a drug delivery system.

Methods: 10 and 15 weight percentages of TiO_2-MCM-41 were synthesized via co-condensation method using cetyl hexadecyltrimethyl ammonium bromide (CTAB) as structure directing agent, tetraethylorthosilicate(TEOS) as silica source and Degussa P-25 as titania source. The characterization of the prepared samples was done by powdered XRD, Fourier Transformed-Infrared spectroscopy (FTIR), scanning electron microscopy (SEM), and DSC. Its drug delivery activity was also studied taking Ibuprofen as test drug.

Results: Characterization result indicated that TiO_2-MCM-41 retained the mesoscopic morphology and porous structure. The results of density and viscosity measurements have been discussed in the light of molecular interactions. It was found that TiO_2-MCM-41 have lower density and viscosity in comparison to parent MCM-41, whereas (15)TiO_2-MCM-41 shows highest solute-solvent interaction and lowest solute-solute interaction in ethanol in presence of nicotinamide and exhibited highest drug release capacity.

Keywords: TiO_2-MCM-41, Ethanol, Nicotinamide, Partial molar properties, Viscosity co-efficient, Drug delivery application.

INTRODUCTION

Nanosized titania is a low-cost, high performance inorganic metal oxide having wide applications like photovoltaic, catalysis, photo catalysis, filtration, sensors, cosmetics, sunscreen lotions, semiconductor. Since its commercial production in the beginning of the twentieth century, it has attracted the attention of researchers for exploring its properties [1-5]. Recently, it has done miracle in the field of medical science, in the treatment of cancer as an improved drug delivery system (DDS) [2] due to its useful properties like water insolubility, non-toxicity, non-radioactivity, biocompatibility, chemical stability, mechanical suitability, etc. It can readily bind a variety of ligands to its surface. This property showed new light to the researchers for an improved drug delivery system for most water insoluble drugs. Incorporation of titania species into mesoporous silica materials has attracted much interest due to high surface area(>200 m^2g^{-1}) in comparison to pure titania. Again, uniform mesopores of MCM-41 control the particle size of TiO_2 and prevent agglomeration of the particles which is the major drawback during the synthesis process. TiO_2 incorporated MCM-41 was first reported in 1994[3]. The inorganic nanoscale titanium dioxide forms Ti-O-Si bond by co-condensation with –OH groups of MCM-41 and exists as a monolayer in the inner walls of TiO_2-MCM-41[4]. The typical structure of this inorganic metal oxide modified TiO_2-MCM-41 mesoporous materials have great potential for applications as effective catalysts, photocatalysts, and electrode materials [5].

Although, both TiO_2 and MCM-41 have proved themselves as effective drug delivery systems [6, 7], however, the drug delivery application of TiO_2-MCM-41 was seldom studied. The present work aims at studying the physico-chemical properties of titania modified MCM-41 and comparing that of MCM-41 reported earlier [8]. In continuation to our work[8],on the volumetric and viscometric study of MCM-41 in presence of nicotinamide (a hydrotropic agent)in ethanol, the present work intends to study the viscosity, density and drug delivery application of (10 wt %,and 15 wt %)TiO_2-MCM-41 in ethanol and compare the results with those of naked MCM-41. The main purpose of this work is to elucidate the molecular interaction that taking place in the system which would be helpful to understand the structural and characteristics properties of these materials providing better scope to use this inorganic mesoporous composite for carriers of partially insoluble drugs.

MATERIALS AND METHODS

Materials

Cetyl hexa decyltrimethyl ammonium bromide (CTAB) (used as structure directing agent), Tetraethylorthosilicate (TEOS) (used as the silica source), ammonia solution (used as mineralizing agent)and nicotinamide used as (hydrotropic agent),sodium hydroxide-hexane were purchased from Merck and Degussa P-25 (as titania source(80% anatase,20% rutile)) was purchased from Sigma-Aldrich. Ethanol was of AnalaR grade and used after drying over molecular sieve over night. Deionized water (Sp. Cond. ~10^{-6} S cm^{-1}) was used throughout the experiment. Ibuprofen (>99.5%) was provided from Aldrich.

Synthesis

The pristine MCM-41 was prepared as reported earlier [8]. Various amounts of titania (0.30g and 0.45g) were added separately to 1.5 g of CTAB in 30 ml deionized water. Then 3 ml of TEOS and 45 ml of ethanol were added and stirred for 30 minutes for hydrolysis.10.1 ml of ammonia solution was added at once to the reaction mixture causing immediate gel formation. The precipitate so obtained in each case was filtered, washed several times with deionized water and dried at 80^0 C for 24 h. Calcination of the samples was carried out at 550^0 C for 5h. The samples are designated as (xx) TiO_2-MCM-41, where xx=10 or15 wt %.

Preparation of solution of TiO_2-MCM-41

The solutions of modified TiO_2-MCM-41 were prepared in 0.1 M nicotinamide in ethanol as solvent. The concentration of the solutions ranges from 40 ppm to 140 ppm, and the solutions were used on the same day.

Measurement of density

The density values of 0.1M nicotinamide in ethanol and the solutions of TiO_2-MCM-41 in 0.1 M nicotinamide in ethanol were determined by relative measurement methods by using specific gravity bottle of 25 ml capacity as described elsewhere[9]. At least five observations were taken and differences between any two readings did not exceed ± 0.02%. Measurement of density was done in the temperature range, 298.15K to 313.15K at 5 K intervals.

Measurement of viscosity

Viscosity measurements on the solutions were made at different temperatures ranging from 298.15K to 313.15K at an interval of 5K in a water thermostat maintained at appropriate temperatures varying within ±0.05K by using an Ostwald Viscometer as described elsewhere[9]. The viscosity values so obtained were accurate to within $\pm 0.3\times10^{-3}$Cp.

The solutions of TiO_2-MCM-41 varied over a concentration range of 40 ppmto140 ppm, i. e., 2.5×10^{-7} to 8.8×10^{-7} M.

Ibuprofen loading and in vitro release measurements

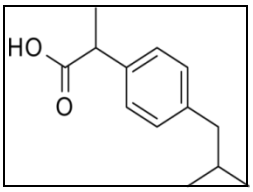
Preparation of standard solutions

In the purpose of calculating the amount of Ibuprofen loaded to MCM-41 and (xx) TiO_2-MCM-41, standard solutions were prepared in the concentrations of 2µg/ml-10µg/ml by appropriate dilutions. Absorbance measurements were recorded between 200-300 nm. The absorbance values at 222 nm were used for the all calculations of the concentration of Ibuprofen. The absorbance values and concentrations of these standard solutions were used to plot the calibration curve. A stock solution was prepared by dissolving 200 mg of Ibuprofen in 250 ml phosphate buffer, pH 7.4. Absorbance at the λ_{max} 222 nm was measured. A calibration curve was plotted between absorbance and concentration.

***In vitro* release studies**

200 mg of MCM-41,and (xx) TiO_2-MCM-41 were conformed into disks by applying pressure (1 ton) and soaked in solutions of ibuprofen in hexane (25 mg/ml) separately for 48 hours so that the absorption process reached 30 wt % with respect to the starting materials. The ibuprofen impregnated samples are designated as MCM-41-Ibu and (xx) TiO_2-MCM-41-Ibu. The concentration of the absorbed ibuprofen in the samples was determined by UV-vis spectrophotometer at a wavelength of 222 nm using Nanodrop spectrophotometer V-630.

The concentration of Ibuprofen (molecular mass=122.12 gm, structure is shown below) was calculated according to the standard curve prepared in the concentration range of 10µg/ml.



Ibuprofen

For in vitro release studies, 200 mg each of MCM-41, and (xx) TiO_2-MCM-41 were compressed into tablet forms having 13 mm diameter by applying 1 ton pressure. The drug release rate from the drug incorporated samples was studied at pH 7.4 using phosphate buffer under sink conditions at 37±0.5ºC in Electro lab Tablet Dissolution Tester Model no. TDT06L. At appropriate time intervals, 2 ml samples were withdrawn and made up to 10 ml by adding buffer, and the drug release was monitored by spectrophotometry as a function of time (for 6 hours) at a wavelength of 222 nm using Nanodrop spectrophotometer V-630.

Theoretical aspects

From the density (d), and viscosity co-efficient (η) data, the following parameters have been determined.

Apparent molar volume, V_φ was calculated by the standard equation (1) [10]

$$V_\varphi=1000(cd_0)^{-1}(d_0-d)+Md_0^{-1} \quad (1)$$

where c is the molar concentration, d_0 is the density of the solvent, d is that of the solution and M is the molecular mass of TiO_2-MCM-41, as determined earlier [8].

Limiting apparent molar volume, V_φ^0 was determined by least square method [10] by fitting the V_φ data to the Masson equation [10] by equation (2)

$$V_\varphi= V_\varphi^0+ S_v c^{1/2} \quad (2)$$

Where, S_v is the slope of the V_φ vs $c^{1/2}$plot.

Apparent molar expansibility E_φ was calculated by using equation [10](3)

$$E_\varphi =E_\varphi^0 + (\alpha-\alpha_0)1000\, c^{-1} \quad (3)$$

where α and α_0 are the co-efficients of expansion of the solution and solvent respectively, and were obtained from the usual relation [10].

Limiting apparent expansibility E_φ^0 was determined by least square method [10] by fitting the E_φ data to the Masson equation [10] by equation (4)

$$E_\varphi= E_\varphi^0+ S_E c^{1/2} \quad (4)$$

where S_E is the slope of the E_φ vs $c^{1/2}$plot.

The viscosity data of the solution were analyzed by Jones-Dole [11] empirical equation as follows

$$\eta_r=\eta/\eta_0=1+A_F c^{1/2}+B_J c \quad (6)$$

where η_r is the relative viscosity, η is the viscosity co-efficient of the solution, η_0 is that of the solvent, A_F is Falken-Hagen co-efficient and B_J is Jones-Dole co-efficient.

The constants A_F and B_J are the intercept and slope of the linear plots of $(\eta/\eta_0-1)/c^{1/2}$ vs. $c^{1/2}$, respectively, and were determined by least squares method [10].

The viscosity data have been analyzed on the basis of transition state theory from the relation [15]

$$\Delta\mu_2^{0*}= \Delta\mu_1^{0*}+ (RT/\bar{V}_1^0)1000B - (\bar{V}_1^0- \bar{V}_2^0) \quad (7)$$

Where, $\Delta\mu_2^{0*}$is the contribution per mol of the solute to free energy of activation for viscous flow of the solution.

$$\Delta\mu_1^{0*}=2.303\, R\, T \log(\eta_0\, \bar{V}_1^0/hN) \quad (8)$$

Where, h and N are Planck's constant and Avogadro number, respectively.

$\Delta\mu_1^{0*}$is the contribution per mol of the solvent to free energy of activation for viscous flow of the solution.

$$V_1^0=M_{solvent}/d \quad (9)$$

$$V_2^0= V_\varphi^0 \quad (10)$$

RESULTS AND DISCUSSION

Characterization of TiO_2-MCM-41

The Scanning Electron Microscopy (SEM) indicated that the presence of 2D hexagonal long range mesoscopic morphology in TiO_2-MCM-41 (fig. 1). The uniform distribution of spherical particles resembling MCM-41[8] represents the siliceous material in the outer surface.

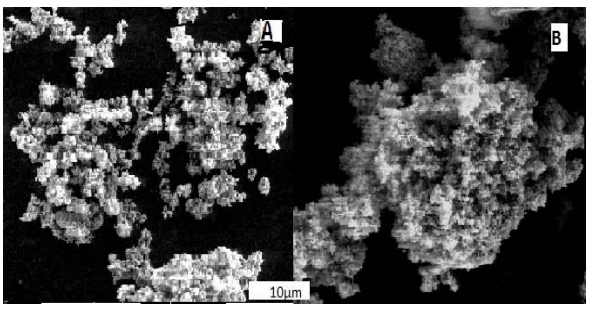


Fig. 1: SEM images of mesoporous (10) TiO_2-MCM-41(A) and (15) TiO_2-MCM-41(B)

MCM-41 and (xx) TiO_2-MCM-41 were also characterized by XRD, FTIR and composite diffractogram which showed the retention of hexagonal siliceous structure and rutile phase of titania in the titania modified samples[13].

Densiometric study

The density of solvent (0.1M nicotinamide in ethanol) and those of the solutions of TiO_2-MCM-41 of different concentrations have been determined at four different temperatures varying from 298.15K to 313.15K. The density values of the solutions of the modified TiO_2-MCM-41 are given in table 1. As observed, the density values of solutions of the modified TiO_2-MCM-41 except at 40 ppm are lower than those of MCM-41[8] at the experimental temperatures. This is reflected in fig. 2(a typical plot of density vs. concentration at 298.15 K). The lowering of density value of the modified MCM-41 with TiO_2(for both the compositions)at high concentrations with the addition of the modified TiO_2-MCM-41to 0.1M nicotinamide in ethanol may be due to the fact that ethanol molecules along with the dissolved nicotinamide because of the smaller size, as compared to the modified TiO_2-MCM-41 causing the latter to swell resulting in the increased volume and hence the density values decrease. The higher density values of (xx)TiO_2-MCM-41 than that of MCM-41 at 40 ppm may be due to the fact that the dissolution of TiO_2-MCM-41 in ethanolic nicotinamide solution is a slow process and occurs in several stages[14]. First, the solvent, ethanol molecules with the dissolved nicotinamide penetrate deep into the TiO_2-MCM-41 to produce a swollen gel, and secondly the strong TiO_2-MCM-41-solvent(ethanol with nicotinamide) interactions overcoming the solute-solute(i. e. TiO_2-MCM-41)intermolecular force of interaction transform the swollen gel into true solution resulting in a decrease in volume thereby increasing the density at 40 ppm of both TiO_2-MCM-41 as compared to that of MCM-41. Further,as TiO_2-MCM-41 proportion increases in ethanolic nicotinamide solution,TiO_2-MCM-41 exists in fully swollen state thereby causing an increase in volume and hence, a decrease in density.

As can be seen from table 1(displayed in fig. 2 at 298.15 K only) the density values for the (xx)TiO_2-MCM-41 decrease with increase in concentration, attain a minima at 80 ppm and then increase at 100 ppm followed by a decrease as the proportion of TiO_2-MCM-41 increases in the mixture. But, (15) TiO_2-MCM-41showed a peculiar behavior where the density increases beyond 120 ppm, i. e., exhibits a second minima at 120 ppm. As usual, the formation of the swollen gel and the transformation of the swollen gel into true solution may be the plausible cause of the decreased and increased density values of the samples, respectively. However, the solutions of MCM-41 behave in a different manner, from those of TiO_2-MCM-41 showing an increased trend in its density values with concentration. It is seen that the density values for all the solutions decrease with increase in temperature.

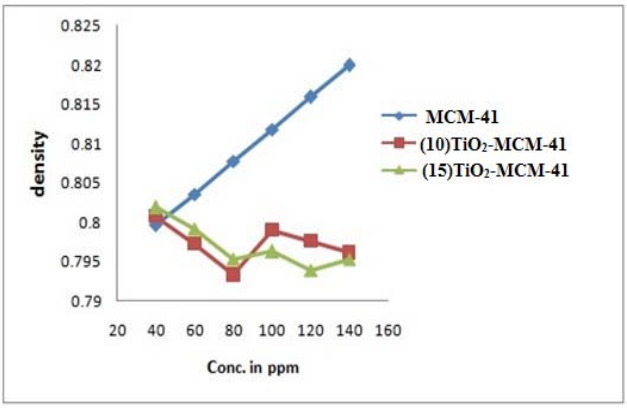


Fig. 2: Plot of density vs. Conc. of solutions of MCM-41, and (xx) TiO_2- MCM-41 at 298.15K

Table 1: Values of densities, d (Kg/m3) of (xx) TiO2-MCM-41 in 0.1 M Nicotinamide in Ethanol at four different temperatures Density of (10) TiO2-MCM-41 in 0.1 M nicotinamide in ethanol

Temp(K)	Concentration (ppm)					
	40 ppm	60 ppm	80 ppm	100 ppm	120 ppm	140 ppm
298.15	0.8008	0.7972	0.7933	0.7990	0.7976	0.7961
303.15	0.7988	0.7967	0.7890	0.7947	0.7939	0.7932
308.15	0.7920	0.7894	0.7881	0.7945	0.7896	0.7892
313.15	0.7891	0.7860	0.7803	0.7929	0.7875	0.7867

Density of (15) TiO_2-MCM-41 in 0.1 M nicotinamide in ethanol

298.15	0.8019	0.7992	0.7953	0.7963	0.7939	0.7956
303.15	0.7991	0.7974	0.7911	0.7937	0.7905	0.7919
308.15	0.7930	0.7904	0.7890	0.7922	0.7881	0.7889
313.15	0.7902	0.7863	0.7843	0.7905	0.7849	0.7853

Using the density values (d) of the solutions and solvent (d_0) in Equation (1), the apparent molar volume (V_φ) was calculated at each concentration(c) of the solutions. The concentration was changed from ppm scale to molar scale. The values of limiting apparent molar volume (V_φ^0) and limiting apparent molar expansibility (E_φ^0) and S_v of MCM-41, and (xx) TiO_2-MCM-41 in 0.1 M nicotinamide ethanolic solutions at 298.15K, 303.15K.308.15K and 313.15K are given in table 2.

Table 2: Values of parameter V_φ ($m^3\ mol^{-1}$),V_φ^0($m^3\ mol^{-1}$), Sv($m^{9/2}\ mol^{3/2}$), E_φ($m^3\ mol^{-1}K^{-1}$), E_φ^0 ($m^3\ mol^{-1}K^{-1}$) and S_E ($m^{9/2}\ mol^{-3/2}K^{-1}$) for solutions of (xx) TiO_2- MCM-41 at different concentrations and temperatures

(10) TiO_2- MCM-41in 0.1 M nicotinamide in ethanol

Temp(K)	$c\times10^7$ moldm^{-3}	$V_\varphi\times10^{-7}$	$V_\varphi^0\times10^{-7}$	$S_V\times10^{-}$[10]	$E_\varphi\times10^{-5}$	$E_\varphi^0\times10^{-6}$	$S_E\times10^{-9}$
298.15	2.423	-2.575			5.397		
	3.635	-0.482			2.677		
	4.847	+0.673	-3.732	4.386	5.313	0.862	0.907
	6.059	-0.644			-5.481		
	7.271	-0.290			0.063		

	8.483	-0.023			4.337		
303.15	2.423	-2.541			5.316		
	3.635	-1.407			2.525		
	4.847	0.960	-5.403	6.464	5.389	1.329	-1.677
	6.059	-0.417			-5.469		
	7.271	-0.204			-0.272		
	8.483	-0.068			-0.607		
308.15	2.423	-1.445			5.680		
	3.635	-0.048			2.791		
	4.847	0.309	-2.004	2.259	5.296	1.381	-1.730
	6.059	-1.090			-5.578		
	7.271	-0.048			0.112		
	8.483	0.110			-0.592		
313.15	2.423	-1.714			5.635		
	3.635	-0.610			2.745		
	4.847	0.757	-3.198	3.835	5.535	1.384	-1.735
	6.059	-1.473			-5.662		
	7.271	-0.276			0.067		
	8.483	0.786			-0.620		

(15) TiO_2-MCM-41 in 0.1 M nicotinamide in ethanol

298.15	2.435	-3.127			5.300		
	3.653	-1.148			6.428		
	4.871	0.149	-5.796	7.112	1.744	1.504	-1.915
	6.088	-0.082			-5.791		
	7.306	0.347			-1.092		
	8.524	0.050			0.301		
303.15	2.435	-3.347			5.262		
	3.653	-1.637			6.361		
	4.871	0.409	-5.857	6.856	2.316	1.511	-1.914
	6.088	-0.207			-5.831		
	7.306	-0.388			-1.091		
	8.524	-0.124			0.315		
308.15	2.435	-1.956			5.502		
	3.653	-0.395			6.702		
	4.871	0.072	-3.307	3.959	2.336	1.5813	-2.0016
	6.088	-0.603			-5.982		
	7.306	0.211			-1.134		
	8.524	0.065			0.313		
313.15	2.435	-2.278			5.558		
	3.653	-0.153			6.640		
	4.871	0.412	-3.84	3.674	2.304	1.5816	-2.0015
	6.088	-1.961			-5.931		
	7.306	0.177			-1.120		
	8.524	0.095			0.314		

A perusal of table 2 shows that the values of V_φ^0 are negative for all the three samples at the experimental temperatures. Since the V_φ^0 is a measure of solute-solvent interaction, the negative values of V_φ^0 indicate weaker solute-solvent interaction [8, 15]. The results indicate that the solute-solvent interactions vary irregularly with increase in temperature supporting to the fact the formation of the swollen gel and the transformation of the swollen gel into true solution are affected more or less with increase of temperature. As observed, the values of V_φ^0 are more negative for both the samples of TiO_2-MCM-41 than that of MCM-41. This point to the fact that the solute-solvent interactions in the former case are weaker as compared to the latter. In other words, the addition of TiO_2 to MCM-41 favors the structure making effect of TiO_2-MCM-41 in ethanol-nicotinamide (hydrotropic agent) mixture.

The positive values of S_V at the experimented temperatures for TiO_2-MCM-41 indicate the presence of solute-solute interaction. The positive values of E_φ^0in TiO_2 modified MCM-41 indicate a possible packing effect involving structure making in these samples. The E_φ^0 values increase with increase in temperature for titania modified MCM-41.

Viscometric study

The experimentally determined values of viscosity (η) and relative viscosities (η_r) of solutions of (xx) TiO_2-MCM-41 at 298.15 K are shown in table 3. As observed from the table, the viscosity values follow the same trend as those of density for Titania modified samples.

Table 3: Values of viscosities η (poise) and relative viscosities (η_r) for solutions of (xx) TiO_2- MCM-41 at different temperatures

(10)TiO_2-MCM-41				**(15)TiO_2-MCM-41**		
Temp(K)	**$c\times10^7$ moldm^{-3}**	**$\eta\times10^3$ poise**	**η_r**	**$c\times10^7$ moldm^{-3}**	**$\eta\times10^3$ poise**	**η_r**
298.15	2.423	10.311	1.049	2.435	10.431	1.061
	3.635	10.212	1.039	3.653	10.387	1.056
	4.847	10.110	1.028	4.871	9.832	1.000
	6.059	10.288	1.047	6.088	11.568	1.177

	7.271	10.218	1.039	7.306	9.845	1.001
	8.483	10.146	1.032	8.524	9.878	1.005
303.15	2.423	9.305	1.050	2.435	9.458	1.067
	3.635	9.230	1.042	3.653	9.338	1.054
	4.847	8.943	1.009	4.871	9.116	1.029
	6.059	9.157	1.033	6.088	10.872	1.227
	7.271	9.098	1.027	7.306	9.109	1.028
	8.483	8.991	1.015	8.524	9.671	1.211
308.15	2.423	8.393	1.051	2.435	8.689	1.088
	3.635	8.271	1.035	3.653	8.566	1.072
	4.847	8.163	1.022	4.871	8.466	1.060
	6.059	8.325	1.042	6.088	10.246	1.283
	7.271	8.175	1.023	7.306	8.588	1.075
	8.483	8.075	1.011	8.524	9.022	1.129
313.15	2.423	7.495	1.048	2.435	7.878	1.102
	3.635	7.381	1.032	3.653	7.707	1.078
	4.847	7.280	1.018	4.871	7.650	1.070
	6.059	7.518	1.051	6.088	9.529	1.333
	7.271	7.379	1.032	7.306	7.999	1.119
	8.483	7.285	1.019	8.524	7.295	1.020

Viscosity data were analyzed by means of Jones-Dole equation using equation 6. The values of viscosity co-efficients A_F, B_J, $\Delta\mu_1{}^{0*}$, and $\Delta\mu_2{}^{0*}$have been evaluated and are presented in Table.

Table 4: Values of parameters A_F ($dm^{3/2}$ $mol^{-1/2}$), B_J (dm^3 mol^{-1}), $\Delta\mu_1{}^{0*}$(kJ mol^{-1}), $\Delta\mu_2{}^{0*}$(Kj Mol^{-1}), and BJ/ $V_\varphi{}^0$ for solutions of MCM-41, (xx) TiO_2-MCM-41 of different concentrations at different temperatures

Parameters	Temp (K)											
	MCM-41				(10)TiO_2-MCM-41				(15)TiO_2-MCM-41			
	298.15	303.15	308.15	313.15	298.15	303.15	308.15	313.15	298.15	303.15	308.15	313.15
A_F	-57.16	-42.19	-36.60	-64.21	148.25	176.06	179.79	150.10	225.55	138.82	196.75	289.3
B_J ×10^{-5}	1.65	1.37	1.49	1.94	-1.24	-1.79	-1.81	-1.37	-2.06	-3.22	-5.55	-1.63
$\Delta\mu_1{}^{0*}$	67.30	68.17	69.02	69.85	67.30	68.17	69.02	69.85	67.30	68.17	69.02	69.85
$\Delta\mu_2{}^{0*}$ ×10^{-}[10]	1.64	1.38	1.53	2.03	-1.20	-1.80	-1.90	-1.40	-2.10	-0.33	-0.57	-1.7
B_J/V^0 ×10^3	-47.3	-35.4	-30.7	-49.3	3.34	3.32	9.06	4.29	3.56	0.55	1.68	4.97

Identical conclusions in regard to solute-solute and solute-solvent interactions are obtained from the viscometric and apparent molar volume data. The negative value of coefficient A_F in MCM-41 indicates the presence of weak solute-solute interaction, which may be attributed to the formation of a sheath of ethanol molecules around the solute resulting in the weakening of solute-solute interaction. The positive and highest value of A_F in (15) TiO_2-MCM-41(except at 303.15K) may be ascribed to the increased solute-solute interactions with increase in titania modification. The positive and highest value of B_J in MCM-41 indicates the presence of solute-solvent interaction owing to the structure making tendency of the solute in the solvent [16, 17]. The behavior of $\Delta\mu_2{}^{0*}$ is similar to B_J. The $\Delta\mu_2{}^{0*}$, the Gibbs free energy of activation for viscous flow of solution is positive and also larger than the free energy of activation for viscous flow of solvent ($\Delta\mu_1{}^{0*}$) for MCM-41 which suggests that there is strong interaction between the solute and solvent molecules in the ground state than in the transition state. The reverse the case is for TiO_2-MCM-41. The solvation can be judged from the hydration number ($B_J/V_\varphi{}^0$) as given in table 4. These negative values indicate that the MCM-41 molecules are less solvated. The $B_J/ V_\varphi{}^0$ becomes positive for (xx) TiO_2-MCM-41This indicates that TiO_2-MCM-41 is more solvated than MCM-41.

Ibuprofen loading and release

Loading of Ibuprofen into mesoporous materials was confirmed by FTIR analysis (fig. 4) using Jasco FTIR (Model 4100,Japan). The presence of carboxyl vibration bands at 1718 cm^{-1}, and C-H stretching vibrations in the 2950-2850 cm^{-1} range from the alkyl groups of ibuprofen, confirmed drug loading into the host matrix. The broad band between 3100-3600 cm^{-1} is due to physically adsorbed water whose intensity is decreased after drug loading which may be due to hydrogen bonding with carboxyl group of Ibuprofen.

The peaks between 1620-1601 cm^{-1} are due to H-O-H stretching vibration in the Si-O-Si structure. The peak at about 950 cm^{-1} is observed for (xx) TiO_2-MCM-41, which is often used as evidence for the vibration of Ti-O-Si confirming to silica–titania inorganic network. A prominent peak near 1680 cm^{-1} is observed in drug loaded samples which may be due to carbonyl group present in Ibuprofen. The compatibility of (xx) TiO_2-MCM-41 in Ibuprofen drug was evaluated through DSC analysis using Mettler Toledo DSC1 instrument. The curves of drug loaded (xx) TiO_2-MCM-41 and blank ibuprofen are presented in Figs 5 and 6,respectively. It was evident from the DSC profile that all the samples exhibited sharp exothermic peaks near 77^{0}C which correspond to the reported melting temperature of the drug.

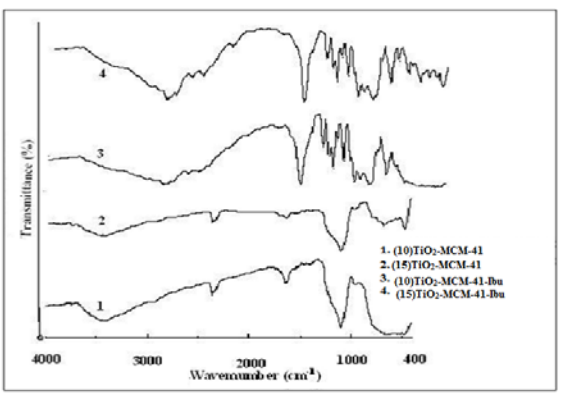


Fig. 4: FTIR image of mesoporous (xx) TiO_2-MCM-41 and drug loaded (xx) TiO_2-MCM-41

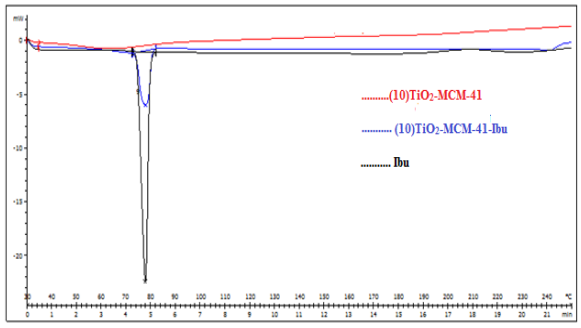


Fig. 5: DSC thermograph of (10) TiO_2-MCM-41, (10) TiO_2-MCM-41-Ibu and Ibu

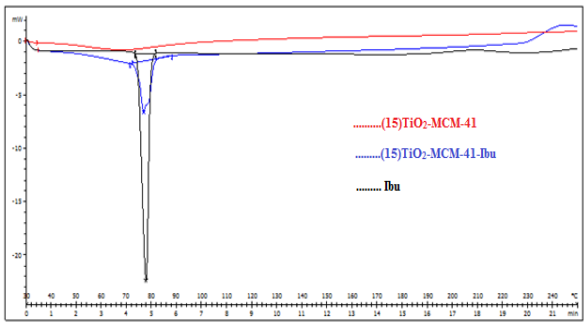


Fig. 6: DSC thermograph of (15) TiO_2-MCM-41, (15) TiO_2-MCM-41-Ibu and Ibu

The Ibuprofen loading was calculated by Beer-Lambert law [18-20]. % of Ibuprofen loaded in the samples (MCM-41 and (xx) TiO_2-MCM-41) were shown in table 5 and fig. 8. From the table, it is found that MCM-41 shows maximum drug loading capacity, and it decreases for the samples coated with TiO_2. This may be due to the reduced specific surface area and pore volume due to titania deposition which results in a decrease in the Ibuprofen loading amount. FTIR study(fig. 4) shows that more silanol(Si-OH) groups are present on the surface of MCM-41 in comparison to titania modified MCM-41, thereby forming more hydrogen bonds with the carboxyl group of Ibuprofen and showing maximum drug loading capacity(Fig.7).

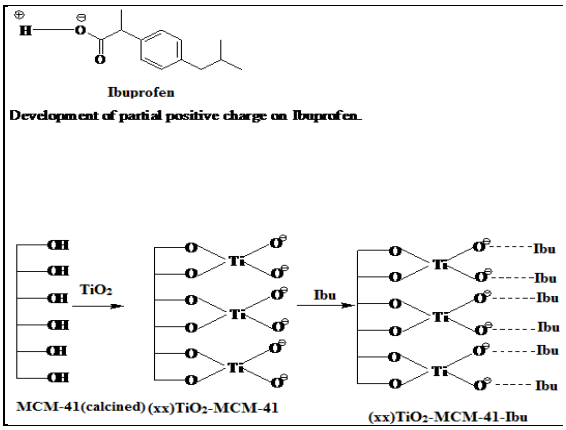


Fig. 7: Mechanism of drug loading

Table 5: Loading of Ibuprofen

Samples	Drug loading (%)
MCM-41	34.22
(10) TiO_2-MCM-41	23.90
(15) TiO_2-MCM-41	19.86

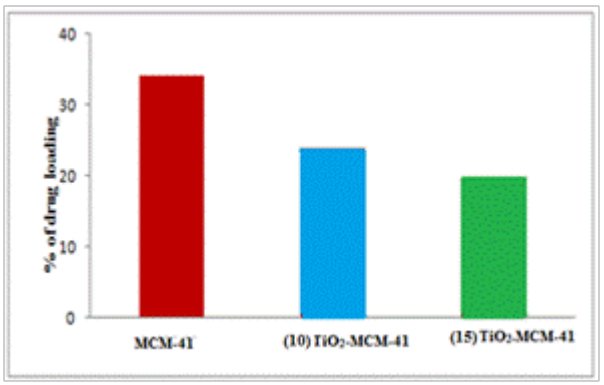


Fig. 8: % of loading of ibuprofen in MCM-41, (10) TiO_2-MCM-41, (15) TiO_2-MCM-41

Fig. 8 shows the percentage of ibuprofen release as a function of time for MCM-41, and (xx) TiO_2-MCM-41 samples loaded with ibuprofen and immersed into buffer solution. It is found that (15) TiO_2-MCM-41 shows highest drug releasing capacity among the three.

This may be due to the weak interaction of drug and TiO_2-MCM-41which results in the increase in drug releasing rate as shown in table 6 and fig. 9.

Table 6: Release of Ibuprofen

Time in min	MCM 41	(10)TiO_2-MCM-41	(15)TiO_2-MCM-41
15	0.901	1.037	1.258
30	1.582	1.871	2.619
45	2.143	2.807	3.164
60	2.841	3.385	4.236
90	3.283	3.759	4.610
120	5.308	6.583	7.094
180	9.459	10.139	10.820
240	12.997	13.355	14.222
300	16.417	17.761	19.768
360	21.861	23.375	25.502

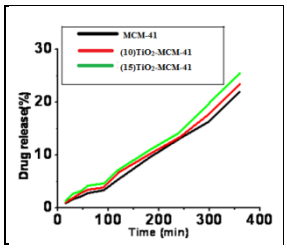


Fig. 9: *In vitro* release of ibuprofen from MCM-41 and (xx) TiO_2-MCM-41 in Phosphate buffer

It should be pointed out that the TiO_2-MCM-41 system still shows an appreciable Ibuprofen storage capacity and release rate, suggesting its potential application in the area of drug delivery and release.

CONCLUSION

Among the three samples; [MCM-41, (xx) TiO_2-MCM-41], (15) TiO_2-MCM-41shows highest solute-solvent interaction and lowest solute-solute interaction in ethanol in presence of nicotinamide and exhibits the highest drug releasing capacity.

CONFLICT OF INTERESTS

Declared None

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