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SYNTHESIS AND CHARACTERIZATION OF MONTMORILLONITE - PLGA COMPOSITE AS DELIVERY VEHICLE FOR EXTENDED RELEASE OF METRONIDAZOLE

Arun Kant and Monika Datta*

Analytical Research Laboratory, Department of Chemistry, University of Delhi, Delhi 110007, India.

***Corresponding Author: Monika Datta**
Analytical Research Laboratory, Department of Chemistry, University of Delhi, Delhi 110007, India.

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ABSTRACT
The aim of the present work is to develop a clay based delivery vehicle for system comprising of Montmorillonite (Mt)-PLGA [poly (D, L-lactide-co-glycolide)] composite material to be used as extended release of an antibiotic drug Metronidazole (MTZ). PLGA-MTZ and Mt-PLGA-MTZ composite material were synthesised using different methodologies including single emulsion solvent evaporation (SESE), double emulsion solvent evaporation (DESE) and double emulsion solvent diffusion method (DESD). The synthesized PLGA-MTZ and Mt-PLGA-MTZ composite has been characterized using analytical techniques including X-ray diffraction (XRD), Thermogravimetric analysis (TGA), Transmission Electron Microscopy (TEM) and Scanning Electron microscopic (SEM) imaging with EDX analysis. The *in-vitro* release behaviour of the drug of pure MTZ, synthesized PLGA-MTZ and Mt-PLGA-MTZ composite by different methodologies were investigated in the simulated gastric and intestinal fluids. In the present case possible bioavailability for pure MTZ, PLGA-MTZ and Mt-PLGA-MTZ composites has been calculated from the *in- vitro* drug release data and compared to the pure MTZ and the commercially available tablets.

KEYWORDS: MTZ, Mt, PLGA, SESE, DESE, DESD and extended release.

INTRODUCTION
Drug delivery refers to approaches for transporting a pharmaceutical material in the body achieves its desired therapeutic effect. One of the delivery vehicles is polymer/clay composites, Polymer/clay composites are a class of hybrid material in which clay or modified clay is dispersed in the polymer matrix. A number of polymers have been investigated for designing drug delivery systems, but PLGA [copolymer of poly (lactide), (PLA) and poly (glycolide), (PGA)] an FDA approved polymer has been most extensively used because of its biocompatibility and biodegradability.[01,02]

This research work aims at developing polymer–Mt composites as carrier for drug/s. Mt is used in pharmaceutical field due to its high specific surface area, high cation exchange and absorption capacity.[03,04] In the present work FDA approved Mt and a non-ionic surfactant Pluronic F68 has been selected because of their structural, biological and industrial importance. Mt-PLGA composite material is being further explored as delivery vehicle for the extended release of antibiotic drug MTZ.[05-07]

The use of antibiotics in human medicine grew very fast since their discovery. Their use as preventive medicine and in the treatment of several infections turned these compounds into some of the most widely popular ones in the human health care.[08] MTZ is an antibacterial agent used in treatment of anaerobic infection.[09,10] It also shows antiprotozoal action, antibacterial and antiameobic action.[11-15] It is used in the treatment of *trichomoniasis* of the genitourinary tract in male and female. In amoebiasis, it is effective at all sites of infections and also used in the treatment of giardiaasis and of Vincent's infection. The usual dose of MTZ for adult and children over 10 years is three times daily after food for 7 to 10 days. In elderly women it used to clear vaginitis, in such case is given as vaginal pessaries in a dosage of daily for 10 to 20 days and it also used for eradication of cysts in symptom less carries, treatment with MTZ three times daily for 5 to 10 days.[16] In view of the above facts, the objective of this work was to synthesize a delivery vehicle using Mt-PLGA composite material as host for extended release of MTZ with possibility of better patient compliance with intake of less number of doses.

MATERIALS AND METHODS

Materials

PLGA, MTZ, PF-68 and Montmorillonite KSF used in the present study were obtained from Sigma Aldrich, St. Louis MO USA and were used without any further purification. Analytical grade, Ortho-phosphoric acid, HCl, KCl, NaOH and KH_2PO_4 was procured from MERCK (Germany). HPLC grade methanol, acetonitrile and water were used for drug estimation by HPLC technique. Millipore (HV 0.45µm and GV 0.22 µm) used in the present study were obtained from Millipore (India) Pvt Ltd Bangalore.

Instruments

UV– Visible spectrophotometer from Analytic Jena equipped with a quartz cell having a path length of 1 cm. HPLC system consisted of a Shimadzu Model DGU 20 A5 HPLC pump, a Shimadzu-M20A Diode Array Detector, Shimadzu column oven CTO-10AS governed by a LC Solution software. X-ray diffraction patterns were recorded on a Philips X' Pert-PRO PMRD (D8 Discover Bruker AXS, Germany), Thermal study were recorded by TGA (SSC/5200 SII Seiko), Scanning Electron Microscopic (SEM) images were recorded using a scanning electron microscope (JEOL JSM-6610LV). TEM images were recorded using TECNAI G2T30 FEI Instrument with an accelerating voltage of 300 KV.

EXPERIMENTAL

Synthesis of Mt-PLGA-MTZ composite

Single emulsion solvent evaporation, double emulsion solvent evaporation and double emulsion solvent diffusion method used to synthesise the PLGA-MTZ and Mt-PLGA-MTZ composites. In SESE and DESD method ethyl acetate (EA) has been used as an organic solvent but in case of DESE method dichloromethane (DCM) has been used as an organic solvent.

In the SESE method Polymer (PLGA) and drug was dissolved in an organic solvent. In other step, the known amount of Mt was added to the aqueous solution of PF-68 and was kept on a magnetic stirrer for about an hour. Polymer-drug solution was gradually added (over a period of 10 to 15 minutes) to the aqueous solution of PF-68 containing dispersed Mt, kept under sonication (50 Hz, using Vibra Cell, Sonics and Materials, Inc.) to make a stable o/w single emulsion.

In case of DESE and DESD method, in first step formation of water in oil (w/o) emulsion where the aqueous solution contains the hydrophilic active component (drug) and the organic phase contains the polymer. The aqueous drug solution was added; drop wise, in to the organic phase containing polymer under high sonication using probe sonicator leading to the formation of w/o primary emulsion. In the second step, in order to make a stable w/o/w double emulsion, polymer-drug primary emulsion was gradually added (over a period of 10 to 15 minutes) to the PF68-Mt aqueous dispersion under continuous sonication. In order to maximize the encapsulation of drug, optimization of various parameters were necessary and therefore, optimization of parameters for all three above mentioned methodologies were performed.

After the formation of a stable emulsion of Mt-polymer drug composite, the organic solvent was evaporated by heating at appropriate temperature for 4 to 6 hr with continuous stirring.

The resultant solution was subjected to centrifugation; the solid residue thus obtained was separated and lyophilized at - 45 °C at a pressure of 46 mTorr using Vir Tis (bench top "K" series) lyophilizer. The polymer drug composite powder thus obtained was utilized for characterization using various appropriate analytical techniques and *in-vitro* drug release studies. The supernatant was utilized for the quantitatively estimation of drug and the encapsulation efficiency was calculated. The *in-vitro* release behaviour of the drug from pure MTZ, the synthesized composites by different methodology was investigated in the simulated gastric and intestinal fluids. The possible bioavailability for pure MTZ and synthesised composite has been calculated from the *in- vitro* drug release data and compared to the pure MTZ and the commercially available tablets.[17]

Quantitative estimation of Metronidazole by HPLC method

HPLC technique was used for the estimation of MTZ content released from synthesized samples in simulated intestinal fluid (pH 7.4) during *in-vitro* drug release studies. Initial HPLC studies were focused on the development of methodology for the determination of MTZ. Acetonitrile and 0.01M phosphate solution (pH 4.7) in 15: 85 volume ratio was used as a mobile phase at 1mL per minute flow rate with column oven temperature of 40°C, detector response was measured at 320 nm. To ensure the validity of Beer-Lambert's law a calibration graph was constructed by plotting area under the peak, observed at 6.5 minutes retention time versus concentration of MTZ.

Stock solution of 100 ppm of MTZ was prepared in simulated intestinal fluid. From this stock solution a series of solutions with various known concentrations were prepared in 25 mL standard volumetric flask using same simulated intestinal fluid. Before injecting the solution in to the HPLC column each sample was filtered through 0.22 µm membrane. The area under the peak as a function of concentration of the drug was found to be linear with slope 6.0739×10^4 and correlation coefficient 0.9996.

Beer – Lambert's law was valid in the concentration range of 1 to 50 ppm of MTZ**.** Concentration of the unknown MTZ in each sample was evaluated with the help of the calibration plot **Fig. 1**.

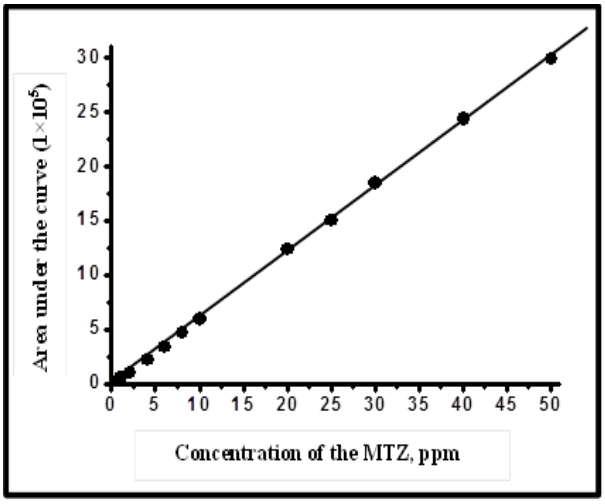


Fig. 1: Instrument response as function of concentration of the MTZ.

Encapsulation efficiency of MTZ in PLGA-MTZ and Mt-PLGA-MTZ composite

The drug encapsulation efficiency is defined as the percentage of initial drug taken retained by the composite and is calculated using the following expression:

$$\text{Encapsulation Efficiency}\,(\%) = \frac{\text{mass of drug retained by the composite}}{\text{initial mass of drug taken}} \times 100$$

The encapsulation efficiency (E.E.) (%) and drug content of the synthesised PLGA-MTZ and Mt-PLGA-MTZ composite to be using SESE, DESE and DESD method was estimated using HPLC are tabulated in Table 1, Table 2 and Table 3.

Table 1: Optimization parameters of encapsulation efficiency and drug loading in synthesised MTZ - PLGA and Mt - MTZ - PLGA composite by SESE method.

Sample Code	Clay, Mt mg	PF68 mg	PLGA mg	MTZ mg	Loading MTZ, %	E. E. MTZ, %
DP 01	-----	50.0	25.0	10.0	6.11	16.17
DP 02	**-----**	**50.0**	**50.0**	**10.0**	**6.08**	**22.41**
DP 03	-----	50.0	100.0	10.0	2.89	21.94
DP 04	-----	50.0	200.0	10.0	0.99	15.69
DP 05	-----	100.0	50.0	10.0	4.66	22.39
DP 06	-----	150.0	50.0	10.0	4.66	22.35
DP 07	-----	200.0	50.0	10.0	4.65	22.32
DP 08	-----	50.0	50.0	15.0	11.78	29.40
DP 09	**-----**	**50.0**	**50.0**	**15.0**	**11.78**	**29.40**
DP 10	-----	50.0	50.0	20.0	8.71	17.36
DP 11	-----	50.0	50.0	25.0	8.76	14.08
DMtP 01	20.0	50.0	50.0	15.0	8.42	23.16
DMtP 02	**50.0**	**50.0**	**50.0**	**15.0**	**7.90**	**30.82**
DMtP 03	100.0	50.0	50.0	15.0	5.06	23.33
DMtP 04	150.0	50.0	50.0	15.0	3.60	21.76
DMtP 05	200.0	50.0	50.0	15.0	2.34	20.39
DMtP 06	50.0	100.0	50.0	15.0	7.89	30.79
DMtP 07	50.0	150.0	50.0	15.0	6.67	30.76
DMtP 08	50.0	200.0	50.0	15.0	5.08	30.72
DMtP 09	50.0	50.0	75.0	15.0	5.62	29.70
DMtP 10	50.0	50.0	100.0	15.0	4.70	28.54
DMtP 11	**50.0**	**50.0**	**50.0**	**20.0**	**14.90**	**35.96**
DMtP 12	50.0	50.0	50.0	25.0	14.70	28.36

Table 2: Optimization parameters of encapsulation efficiency and drug loading in synthesised MTZ-PLGA and Mt-MTZ-PLGA composite by DESE method.

Sample Code	Clay, Mt mg	PF68 mg	PLGA mg	MTZ mg	Loading MTZ, %	E. E. MTZ, %
DP 01	**-----**	**50.0**	**25.0**	**10.0**	**10.98**	**20.87**
DP 02	-----	50.0	50.0	10.0	2.76	11.32
DP 03	-----	50.0	100.0	10.0	0.88	7.02
DP 04	-----	50.0	200.0	10.0	0.57	9.18
DP 05	-----	100.0	25.0	10.0	7.45	20.86
DP 06	-----	150.0	25.0	10.0	6.95	20.84
DP 07	-----	200.0	25.0	10.0	6.61	20.81
DP 08	**-----**	**50.0**	**25.0**	**15.0**	**11.23**	**20.96**
DP 09	-----	50.0	25.0	20.0	8.50	11.69
DP 10	-----	50.0	25.0	25.0	10.18	11.61
DMtP 01	50.0	50.0	25.0	15.0	2.63	8.64
DMtP 02	**100.0**	**50.0**	**25.0**	**15.0**	**2.89**	**17.87**
DMtP 03	150.0	50.0	25.0	15.0	1.69	15.03
DMtP 04	200.0	50.0	25.0	15.0	1.04	13.11
MtP 05	100.0	50.0	25.0	15.0	2.78	17.87
DMtP 06	100.0	50.0	50.0	15.0	2.78	17.97
DMtP 07	100.0	50.0	75.0	15.0	2.77	17.85
DMtP 08	100.0	50.0	100.0	15.0	2.77	17.83
DMtP 09	100.0	100.0	50.0	15.0	5.42	17.96
DMtP 10	100.0	150.0	50.0	15.0	5.39	17.93
DMtP 11	100.0	200.0	50.0	15.0	5.36	17.89
DMtP 12	**100.0**	**50.0**	**25.0**	**20.0**	**4.20**	**18.93**
DMtP 13	100.0	50.0	25.0	25.0	2.80	10.14

Table 3: Optimization parameters of encapsulation efficiency and drug loading in synthesised MTZ-PLGA and Mt-MTZ-PLGA composite by DESD method.

Sample Code	Clay, Mt mg	PF 68 mg	PLGA mg	MTZ mg	Loading MTZ, %	E.E. MTZ, %
DP 01	------	50.0	25.0	10.0	6.35	14.85
DP 02	**------**	**50.0**	**50.0**	**10.0**	**6.39**	**21.29**
DP 03	------	50.0	75.0	10.0	2.05	16.43
DP 04	------	50.0	100.0	10.0	1.05	16.68
DP 05	------	100.0	50.0	10.0	5.26	21.17
DP 06	------	150.0	50.0	10.0	5.25	21.11
DP 07	------	200.0	50.0	10.0	5.23	21.06
DP 08	**------**	**50.0**	**50.0**	**15.0**	**7.78**	**25.19**
DP 09	------	50.0	50.0	20.0	3.25	16.23
DP 10	------	50.0	50.0	25.0	3.19	12.79
DMtP 01	40.0	50.0	50.0	15.0	4.77	11.20
DMtP 02	50.0	50.0	50.0	15.0	6.81	21.94
DMtP 03	**100.0**	**50.0**	**50.0**	**15.0**	**5.85**	**30.93**
DMtP 04	150.0	50.0	50.0	15.0	1.89	16.49
DMtP 05	200.0	50.0	50.0	15.0	1.24	14.93
DMtP 06	100.0	100.0	50.0	15.0	5.25	30.89
DMtP 07	100.0	150.0	50.0	15.0	5.25	30.87
DMtP 08	100.0	50.0	75.0	15.0	3.29	32.49
DMtP 09	100.0	50.0	100.0	15.0	2.66	30.96
DMtP 10	100.0	50.0	75.0	15.0	2.99	32.49
DMtP 11	**100.0**	**50.0**	**75.0**	**20.0**	**4.20**	**36.37**
DMtP 12	100.0	50.0	75.0	25.0	2.80	24.70

In order to maximize the encapsulation of drug, optimization of various parameters were necessary and therefore, optimization of parameters for all three above mentioned methodologies were performed. Drug encapsulation efficiency and drug loading was also evaluated. Optimized parameters of PLGA-MTZ composite and Mt-PLGA-MTZ composite which was synthesized by mentioned three methods are bold, highlighted and listed in given Tables 1, Table 2 and Table 3. These bold and highlighted composites were characterized using appropriate analytical techniques and were also used for *in-vitro* drug release studies.

RESULTS AND DISCUSSION

X-Ray diffraction (XRD) studies

XRD provides important information about clay and its polymer composite material. The XRD pattern of pristine Mt shows characteristic diffraction peak of 001 plane at 2θ value of 6.02° corresponding to basal spacing (d) of 14.66 Å. The XRD pattern of pure MTZ shows strong diffraction peaks at 12.15 º, 13.85 º, 24.62 º, 25.34 º, 27.28º, 29.30 º, 33.34 º indicate crystalline nature of MTZ.[18]

In case of Mt-PLGA-MTZ composite characteristic diffraction peak with low intensity at 4.07° corresponding to 001 plane with d spacing of 21.68 Å was observed so can say that intercalation of PLGA-MTZ moiety in interlayer of Mt. One of the most important facts also seen in the case of Mt-PLGA-MTZ composite, intensity of Mt peak seems to be disappearing suggesting may be exfoliation of Mt layers or it becomes amorphous in nature, **Fig. 2**.

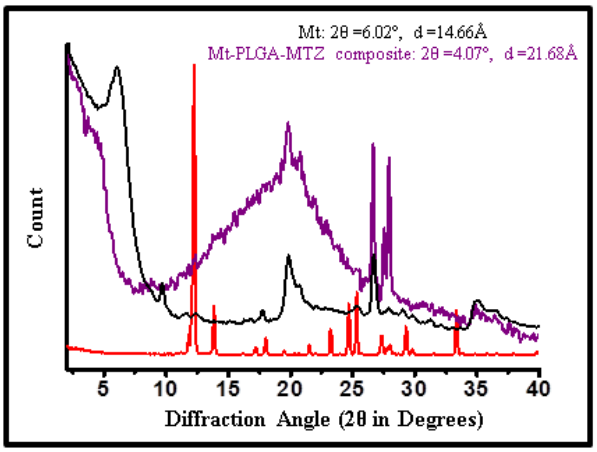


Fig. 2: XRD patterns of Mt, MTZ and Mt-PLGA-MTZ composite.

Thermal studies (TGA)

The TGA thermogram of Pristine Mt, pure drug and Mt-PLGA-drug composite were characterized by TGA to evaluate their thermal behavior in the range of 25°C to 900°C, **Fig. 3**. It is further utilized to investigate the properties of drug interaction with Mt-PLGA composites. Mt show three weight loss, the first weight loss of 17.88% observed between 27°C and 102°C was attributed to the removal of physically adsorbed water. The second weight loss of 9% between 200°C to 430°C is attributed to the loss of structural interlayer water followed by third weight loss of 9% between 550°C to 770°C corresponds to dehydroxylation.[19,20]

PLGA indicate single step mass loss 96% between 210°C to 362°C, These weight losses have been assigned to the total degradation of the material. PF-68 also show single step weight loss 92% between 315°C to 435°C indicate total degradation of surfactant.[21] MTZ show two weight

loss, the first weight loss of 88% between 30°C to 266 °C was attributed to the total degradation of aromatic skeleton and second weight loss 11% between 266°C to 556°C indicate loss of black residue of drug.[22] In case of Mt-PLGA-MTZ composite three weight losses has been assigned, the first weight loss of 12% observed between 31°C to 149°C was attributed to the interlayer water molecule, the second weight loss of 16% between 184°C to 354°C is attributed to the loss of MTZ and surfactant molecule, followed by third weight loss of 3% between 451°C to 672°C corresponded to decomposition of PLGA polymer.

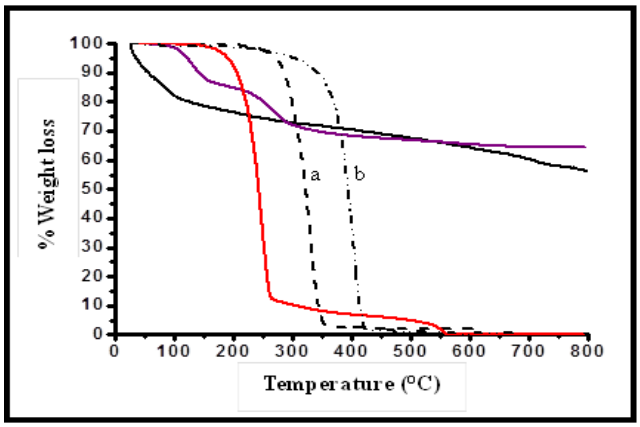
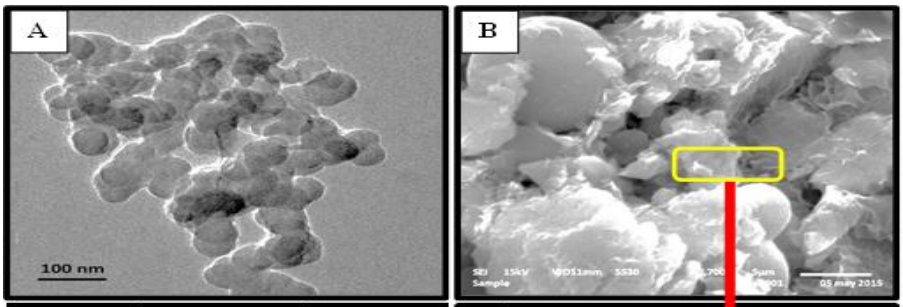


Fig. 3: TGA Thermograms of Mt, PLGA (a), PF-68 (b), MTZ and Mt-PLGA-MTZ composite.

Electron microscopic (TEM and SEM) imaging with EDX analysis

Surface morphology of PLGA-MTZ and Mt-PLGA-MTZ composite was analysed by SEM with energy dispersive X-ray. SEM provides important information about surface morphology of clay and its composite material. TEM also provide the significance properties about exfoliation as well as intercalation properties of clay in the composite material.

In the SEM image of Mt-PLGA-MTZ composite appears to be randomly arranging layered surface with spherical shape of PLGA particles however in TEM it has spherical particle of 50 nm size, **Fig. 4**. The presence of additional peaks of nitrogen in composite along with oxygen, silicon, aluminium, iron and magnesium (EDX analysis) can be taken as an evidence for the presence of MTZ in the Mt-PLGA-MTZ composite.



Elements	Weight%	Atomic%
C	15.06	22.03
N	2.31	2.90
O	47.05	53.08
Fe	1.78	0.74
Mg	1.06	0.47
Al	7.39	4.81
Si	25.35	15.97

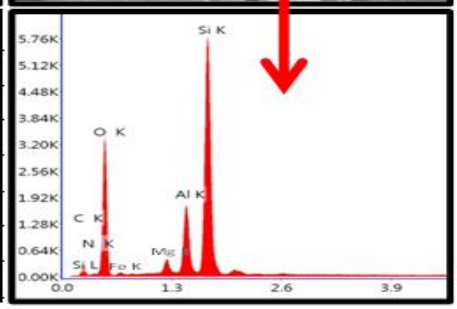


Fig. 4: TEM (A) and SEM (B) image with EDX graph of Mt-PLGA-MTZ Composite.

***In vitro* drug release behavior**

In-vitro release behavior of pure MTZ, PLGA-MTZ and Mt-PLGA-MTZ composite (All three composite synthesized by SESE, DESE and DESD method) was carried out in the simulated gastric fluid (pH 1.2) and intestinal fluid (pH 7.4) using dialysis bag method[23] for a period of 12 hr and it extended up to 36 hr and then 60 hr.

In the simulated gastric fluid pure MTZ release of 71% and 76% in the initial 2 hr, 6 hr respectively after that it becomes constant. In the simulated intestinal fluid pure MTZ release of 89% and 98% of the drug in the initial 2 hr, 3 hr and 30 minute respectively after that it becomes constant.[24] In case of PLGA-MTZ composite, in the simulated gastric fluid a release of 3.97, 4.24 and 6.51% of the MTZ in the initial 2 hr; 9.55, 9.23 and 14.09% over a period of 12 hr; 12.74, 11.96 and 16.97% of the MTZ in 36

hr and followed by a relatively slow cumulative release of 13.51, 12.68 and 17.40% of the MTZ in 60 hr was observed from composite synthesized by SESE, DESE and DESD method respectively after that it becomes constant. In the simulated intestinal fluid a release of 12.30, 12.46 and 13.92% of the MTZ in the initial 2 hr.; 14.99, 15.21 and 17.06% over a period of 12 hr; 16.19, 16.77 and 18.21% of the MTZ in 36 hr; and followed by a relatively slow cumulative release of 16.82, 17.87 and 18.89% of the MTZ in 60 hr was observed from composite synthesized by SESE, DESE and DESD method respectively after that it becomes constant **Fig. 5**.

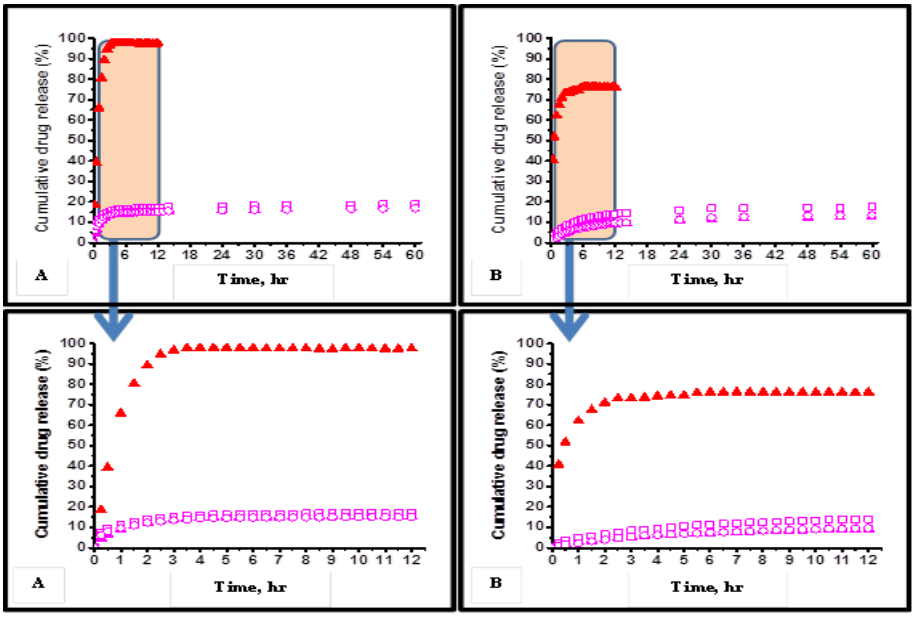


Fig. 5: Drug release behavior in simulated gastric (A) and intestinal fluid (B)
MTZ (▲) and PLGA-MTZ composite, DESE (▲), DESD (□) and SESE (○)

In case of Mt-PLGA-MTZ composite, in the simulated gastric fluid a release of 18.21, 29.99 and 22.82% of the MTZ in the initial 2 hr; 31.18, 40.27 and 34.28% over a period of 12 hr; 32.48, 44.21 and 38.49% of the MTZ in 36 hr and followed by a relatively slow cumulative release of 33.26, 44.86 and 39.83% of the MTZ in 60 hr was observed from composite synthesized by SESE, DESE and DESD method respectively after that it becomes constant. In the simulated intestinal fluid a release of 14.59, 50.37 and 51.71% of the MTZ in the initial 2 hr; 22.55, 61.75 and 63.47% over a period of 12 hr; 23.63, 76.33 and 72.87% of the MTZ in 36 hr and followed by a relatively slow cumulative release of 24.21, 77.70 and 79.31% of the MTZ in 60 hr. was observed from composite synthesized by SESE, DESE and DESD method respectively after that it becomes constant, **Fig. 6**. On the basis of the *in-vitro* drug release studies it has been observed that the Mt-PLGA-MTZ composite provides an extended release delivery of MTZ which is likely to reduce the frequency of drug intake.

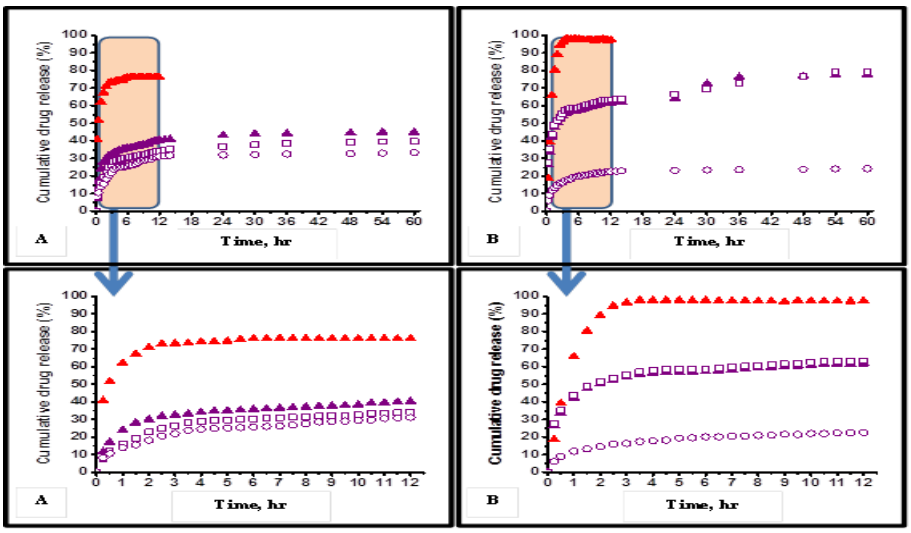


Fig. 6: Drug release behavior in simulated gastric (A) and intestinal fluid (B)
MTZ (▲) and Mt polymer-MTZ composite, DESE (▲), DESD (□) and SESE (○)

Bioavailability of synthesised composite

The bioavailability of PLGA-MTZ composite prepared by SESE, DESE and DESD method is 14.4%, 14.4% and 15.8% respectively and in the case Mt-PLGA-MTZ composite obtained by SESE, DESE and DESD method is 18.9%, 43.4% and 49.3% respectively. Bioavailability of MTZ is not increased in case of PLGA-MTZ but have the potential to extend the release up to 60 hr as compare to the pure MTZ and commercial available tablet.[25] Bioavailability of MTZ is increased in case of Mt-PLGA-MTZ and has the potential to extend the release up to 60 hr as compare to the pure MTZ and commercial available tablet, **Table-4**. Mt-PLGA-MTZ composite as compare to pure MTZ, bioavailability of MTZ is increased by 1.5 and 1.7 times in case of the composite synthesized by the DESE and DESD method respectively. It has been observed that, compared to the commercially available tablets (Flagyl and Metrogyl) performance of the synthesised composite material (Mt-PLGA-MTZ synthesized by the DESE and DESD method) has not only been found superior in terms of probable % bioavailability but also in terms of availability of the drug in the system for a longer period of time.

Table 4: Comparison of bioavailability of drug in various synthesised compositions.

BIOAVAILABILITY OF PURE DRUG, COMMERCIALLY AVAILABLE FORMULATIONS AND SYNTHESISED COMPOSITES MATERIAL, %									
DRUG	PURE DRUG AND COMMERCIAL DRUG			SYNTHESISED PRODUCT					
				PLGA-MTZ composite			Mt-PLGA-MTZ composite		
MTZ	Pure	Metrogyl	Flagyl	SESE	DESE	DESD	SESE	DESE	DESD
	*28.4	**42.9**	40.3	14.4	14.4	15.8	18.9	43.4	49.3

CONCLUSION

The PLGA-MTZ composite and Mt-PLGA-MTZ composite was successfully prepared by three methodology of SESE, DESE and DESD. Encapsulation Efficiency of PLGA for MTZ was found to be 29.40%, 20.94% and 25.19% for the synthetic methodology of SESE, DESE and DESD and respectively. Encapsulation Efficiency of Mt-PLGA composites for MTZ was found to be 35.96%, 18.93% and 36.37% for the synthetic methodology of SESE, DESE and DESD respectively. *In-vitro* drug release behaviour of the process for the antibiotic drug, MTZ, PLGA-MTZ composite and Mt-PLGA-MTZ composite was studied in the simulated gastric and intestinal fluid. Release profile of the PLGA-MTZ and Mt-PLGA-MTZ composites synthesized by SESE, DESE and DESD method is slow and extended manner as compare to pure MTZ. It was observed that the Mt-PLGA-MTZ composite can provide much bioavailability of the drug as compared to the pure MTZ and commercially available tablet (Metrogyl and Flagyl). Mt-PLGA-MTZ composite as compare to pure MTZ, bioavailability of MTZ is increased by 1.5 and 1.7 times in case of the composite synthesized by the DESE and DESD method respectively. Thus on the basis of the present results, it can be concluded that PLGA-MTZ and Mt-PLGA-MTZ composites may have suitable drug delivery vehicle and potential to minimize the dosing frequency and may result in better patient compliance.

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