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Synthesis, Characterization and Evaluation of Poly(3-N,N'-Dimethylaminopropylmethacrylamide-*Co*-2-Hydroxyethylmethacrylate-*Co*- N-Vinyl Pyrrolidone), A Thermo Responsive Hydrogel Carrier For Sustained Release Of Theophylline

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Abstract

Aim : The objective of this investigation is to synthesis and characterize a thermo responsive N,N'-methylene bisacrylamide(MBAA)/ethylene glycol dimethacrylate (EGDMA) crosslinkedpoly([3-N,N'-dimethylamino-propyl]methacrylamide)(DMAPMA)-*co*-2-hydroxy-ethyl methacrylate(HEMA)- *co*-N-vinylpyrrolidone(NVP)) hydrogel for using as a drug carrier for controlled *invitro* release of theophylline(THP) under simulated intestinal and gastric fluids(SIF & SGF).

Methods: The thermoresponsive hydrogel was synthesized in aqueous medium by radical copolymerization of the monomers DMAPMA, HEMA and NVP with the crosslinker MBAA / EGDMA and evaluated as a carrier for *in-vitro* release of theophylline in SIF and SGF. The structure (FT-IR (Fourier transform infra-red) spectroscopy), thermal stability (Thermogravimetric analysis(TGA)/derivative thermogram (DTG), morphology(X-ray diffractogram(XRD), swellability in SIF (at 20-70^{o}C),cytotoxicity on mouse embryonic fibroblast (NIH3T3)cells of this hydrogel and its interaction with THP were analyzed

Results and Conclusion: FT-IR and TGA study revealed that the copolymer contains the monomers and crosslinker residues and is thermally stable respectively. The decreased amorphous character of the hydrogel with the increased DMAPMA content in the monomer feed was more likely attributed to the low molecular weight of the polymer hydrogel by the DMAPMA catalyzed decomposition of persulphate. The hydrogel has thermoresponsive swellability and negligible cytotoxicity. THP release studies revealed both Fickian and anomalous diffusion mechanisms. H-bond modeling by density functional theory on carrier-drug system revealed H-bonding interaction The observed results indicated that this copolymer hydrogel can be function as a viable thermo responsive carrier for controlled and targeted release of drugs by diffusion mechanisms

Keywords: Temperature Sensitive Polymer Hydrogels; NIH-3T3 Cells; Cytotoxicity; Density Functional Theory; *In Vitro* Drug Release.

INTRODUCTION

The slow release of drugs immobilized in a matrix helps to provide a controlled dose at a therapeutic level, ensuring the optimum performance of that drug and helping to achieve the desired physiological outcome with minimum side effects. Controlled drug delivery systems that deliver the active pharmaceuticals at predetermined rates for predefined period of times, have been employed to overcome the shortcomings in delivery of conventional drug formulations. Polymer based oral drug delivery system are increasingly being used to achieve sustained and site specific therapeutic delivery of active biomolecules with increased efficacy [1-2]. Among the polymer carriers, biocompatible polymer hydrogels particularly with stimuli responsive features are investigated as prominent delivery system for targeted delivery to treat many clinical disorders due to their biocompatibility. Eventhough significant progress has been made through this approach, there are ample scope for further advances to be made for treating diverse health problems. The temperature dependent hydrogen bonding and hydrophobic interactions and phase transition behavior of thermoresponsive hydrogels may facilitate them as promising carriers for controlled drug delivery with improved efficacy[3.4]. Hence in the present investigation a copolymer hydrogel from the hydrophobic monomer N-[3-dimethylamino-propyl] methacrylamide (DMAPMA), to instill thermal phase transition behavior and hydrophilic monomers 2-hydroxyethyl methacrylate) and N-vinyl pyrrolidone (NVP) to impart biocompatibility[5-7] was synthesized and evaluated as a thermoresponsive hydrogel carrier taking theophylline (THP) as model drug. It is to be noted that the introduction of NVP and HEMA moieties in the copolymer may improve the mechanical strength of DMAPMA copolymer hydrogels through physical crosslinking such as H-bonding. As a prelude to understand the release mechanism, drug-polymer interaction was also studied by density functional theory (DFT) method .

MATERIALS AND METHODS

Materials

Monomers HEMA (99%), NVP (99%) and DMAPMA (99%) were purchased from Sigma-Aldrich and freed from inhibitors by passing through activated basic alumina column. N,N'- methylene bisacrylamide (BMAA, 99%) and ethyleneglycol dimethacrylate (EGDMA, 98%) from Sigma- Aldrich and potassium persulfate (KPS, 98%, Nice Chemicals) were purified as per standard procedures [8] and used. Methanol, acetone, sodium chloride, hydrochloric acid, monobasic and dibasic sodium phosphate, pepsin, (3-[4, 5-dimethyl thiazol-2-yl] 2, 5-diphenyltetrazolium bromide) (MTT) and the model drug THP (Himedia) were used as received. The mouse embryonic fibroblast NIH-3T3 cell was obtained from the National Centre for Cell Science (NCCS), Pune. The chemical structures of drugs and monomers are given in Fig. 1. Simulated intestinal fluid(SIF, pH=7.2) and simulated gastric fluid (SGF, pH =1.2) were prepared as per United States Pharmacopoeia[9].

Synthesis of hydrogel

The hydrogels were prepared by radical copolymerization of DMAPMA, HEMA and NVP monomers in water solution(10 ml) with KPS initiator and BMAA /or EGDMA crosslinker taken in a 50 ml borosilicate tube at 70°C in a water thermostat (Refrigerated Heating Circulator, Julabo F25 ME) for 10 min after deaeration by purging with nitrogen. The concentrations of the ingredients in the polymerization recipe are furnished in Table 1. The percent conversion was limited to > 95%. The formed polymer gels were washed with excess of ultrapure water and methanol. Then it was cut into small pieces and immersed in water for 48h to remove oligomers, unreacted monomer and

initiator if any. The samples were dried to constant weight at 60°C under vacuum for five days. The dried polymer gels were powdered in a mortar and pestle aand Soxhlet extracted to remove traces of monomers if any and dried in vacuum for 15h. Then finely powdered again in a mortar and pestle, sieved in 150 micron sieves (Jayant Test Sieves, India), and then desiccated for further use.

Polymer characterization

The synthesized polymer carrier was characterized for its swellability, structure, thermal stability, morphology, biocompatibility, drug release characteristics and drug-polymer interaction in SGF and SIF as described below.

Swelling study

The dynamic absorption of fluid was analyzed gravimetrically by immersing 150 mg of the polymer in 50 ml SIF and SGF at 37°C weighing the swollen polymer at known intervals of time using five decimal electronic balance (Mettler Toledo AB265-S) after wiping the sample surface with tissue paper to remove the adhering fluid. The percentage fluid uptake (% degree of swelling) (as average of three measurements ± 0.003 SEM) was calculated using the eq. (1).

$$\% \text{ Fluid uptake} = (W_t - W_0 / W_0)\,\text{x}100 \qquad (1)$$

where W_t is the weight of the swollen polymer at time 't' and W_0 is the initial weight of the dry polymer. For the thermo-responsive studies, the polymer was allowed to equilibrium swelling (48h) in water at different constant temperatures in a thermostat (Julabo F25 ME) for the temperature range 20–70°C and the swelling ratio (W_t/W_0) (an average of three measurements ±0.003 standared error of mean(SEM))was determined for each temperature as described above.

Fourier transform infrared (FT-IR) spectra

FT-IR spectra of the virgin polymer and polymer-drug (tablet) before and after swelling in water were recorded on JASCO FT-IR-460 in KBr matrix (5 mg polymer per 100 mg KBr) for the spectral width 4000-400cm^{-1}. The resolution and number of scans were 2cm^{-1} and 48 respectively.

Thermogravimetry/Derivative thermogravimetry (TG/DTG)

TG/DTG traces of the polymers were recorded under nitrogen on TGA Q500 V20.10 Build 36 at a heating rate of 10°C / min. The sample size was in the range 3-8 mg.

Differential scanning calorimetry (DSC)

DSC traces were recorded on DSC-60 Plus Shimadzu Corporation using uniformely powdered 3 mg dry samples of polymer hydrogel, polymer-drug mixture and drug at 10°C/min under a nitrogen (30ml/min) for the temperature range 50 to 400°C.

X-ray diffractogram (XRD)

XRD was recorded on Shimadzu XRD-6000 diffractometer with CuK_α radiation operated at 40 kV voltage and 30 mA current for the 2θ values 5–70°at a scan speed of 5°/min.

In vitro cytotoxicity studies

This study was conducted in the animal cell culture laboratory of Kovai Medical Centre and Hospital, Coimbatore, India, using the NIH 3T3 mouse embryonic fibroblasts cell line (NIH 3T3) grown in Dulbecco's Modified Eagles Medium containing 10 % fetal bovine serum (FBS) via direct method using optical microscope and also by indirect MTT assay method as per the reported procedure[10] and the average cell viability for 4 measurements was determined for each polymer concentration used.

Ultraviolet (UV) spectra

UV spectra of the pure THP solution[11] and that of the same released from the tablet in drug dissolution studies were recorded on Perkin Elmer Lambda 35 UV-VIS spectrophotometer at 271nm.

Tablet preparation

In a typical tablet (2.5 mm thickness and 13 mm diameter) formulation 200 mg of sieved dry copolymer hydrogel and 15 mg of THP were weighed and mixed homogeneously by grinding them in mortar and pestle, and subsequently compressed using a KBr press (Techno Search M15) at 10 ton pressure. A pure copolymer pellet of the above dimensions was also fabricated similarly without drug for swelling studies.

In vitro drug dissolution

In vitro drug dissolution studies were carried out in an USP apparatus Type II (Veego Model VDA- 6DR) in SGF and SIF at 37°C by embarking the compressed tablet (215 mg) inside the rotating (50 RPM) basket immersed in a thermo stated SGF/ or SIF. The tablets retained their integrity and shape during the entire period of the swelling study. The amount of drug released was estimated UV-spectrophotometrically by withdrawing aliquots of sample from the drug release vessel at different known time intervals and measuring its absorbance at 271nm. An average (x)of three identical experiments was taken (x ± 0.005 SEM)as the amount of drug released for a given set of experimental conditions. To maintain the volume of the experimental solution constant, a volume equivalent of aliquot sample as incubated fresh fluids was added to the solution after each withdrawal.

THP –polymer hydrogel interaction using Gaussian tool

The various reasonable physical structures of poly (DMAPMA-co-HEMA-co- NVP) in the presence and absence of hydrogen bonding with THP were generated using the software Gauss View 5.0.8. Their energies were then computed using B3LYP/ 6-31(d,p)[12,13] affter optimizing their input structures using the software B3LYP/6-31G (d). The resulting output energy which is in the atomic unit (au), was converted into kJ/mol (1 au = 2619.6 kJ/mol).

To compute the polymer-THP interaction energy (ΔE), the energies of the individual polymer and THP molecules and polymer-THP complex were calculated. The hydrogen-bond stabilization energy (ΔE) for the polymer-THP complex is given by equation [14].

$$\Delta E = E_{polymer} + E_{THP} - E_{polymer\text{-}THP\ complex} \qquad (3)$$

In the molecular structure specification section of Gaussian calculation[15], the H- bond between hydrogen atom (hydrogen-bond donor) with oxygen and nitrogen atoms (H-bond acceptor) in the polymer-THP complex was defined for geometry optimization (Fig. 2) involving H- bond interactions.

RESULTS AND DISCUSSION

Preparation of Poly(DMAPMA-co-HEMA-co-NVP)

The radical copolymerization mechanism for the formation of the crosslinked copolymer, poly (DMAPMA-*co*-HEMA-*co*-NVP) is shown in the Fig.3.

Swelling study

The ability of a drug carrier to absorb water is an important aspect to be investigated for drug delivery applications. To evaluate this property, swelling studies were carried out for crosslinked poly(DMAPMA-*co*-HEMA-*co*-NVP) hydrogels at 37°C. The degree of swelling in SGF and SIF for crosslinked hydrogel prepared with various concentrations of DMAPMA for fixed concentrations of HEMA, NVP and BMAA or EGDMA were presented in Figure 4a. No significant difference in the degree of swelling in SGF and SIF for a matrix of typical composition was observed and the pH of a medium doesn't have much effect on the degree of swelling. The temperature response on hydrogel swelling displayed in Fig. 4b indicated that the

polymer shrinks at 35–45°C and then starts swelling after 45°C [16]. The analysis of the plots in Fig. 4b also showed that the degree of swelling of hydrogels with crosslinkers (BMAA and EGDMA) decreased slightly in the temperature range 20-35°C, unlike that for the temperature range 35-45°C, where a drastic increase in degree of swelling was observed with leveling off after 50°C indicating phase-transition behavior[17]. This was more likely due to the presence of hydrophilic and hydrophobic moieties in the polymer backbone. Since swelling and shrinking occur over a relatively narrow temperature range (35-45°C), the drug carrier may be used to release the drug at a specific temperature.

FT-IR spectra

FT-IR spectra of crosslinked polymer carrier and polymer-drug tablet before and after swelling in water are shown in Fig. 5 & 6. The spectra of crosslinked hydrogel carriers (Figs. 5a & 6a) have shown absorptions peaks at 3413 [ν(OH)], 2924 [ν(CH_2)s, ν(CH_3)s], 2853 [δ(CH_3)], 1723 [ν(C=O)], 1656 [ν(C=O) in amide], 1631[ν(NH)s amide I], 1536[in plane δ(NH) amide II], 1398[ν(CH_3)s in N-isopropyl group], 1260 [ν(C-O)] and 1032 [ν(C-O), ester]cm^{-1}. The absorption peaks around 1715 and 1667cm^{-1} in theophylline tablet(Figure 5b) are due to the stretching vibrations of ester -C=O and amide -C=O groups respectively [16-18] . The distinct peaks at 1723 and 1709 cm^{-1} attributed to carbonyl groups in the polymer become single peak at 1715cm^{-1} both in the IR spectra of tablet and tablet made from the swollen polymer gel after drying. These tend to indicate the presence of H-bonding involving C=O and OH groups (C=O----H-O).

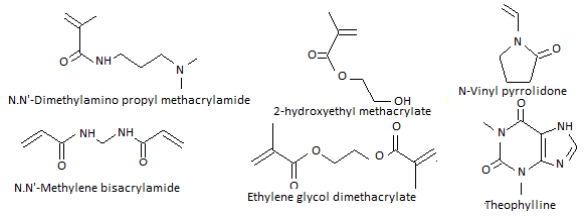


Fig. 1 Molecular structures of monomers, crosslinkers and drugs

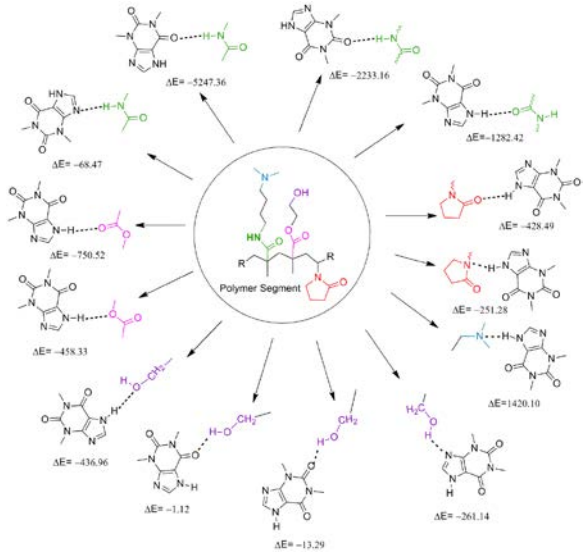


Fig. 2 Modeling of H-bond interaction in polymer-THP

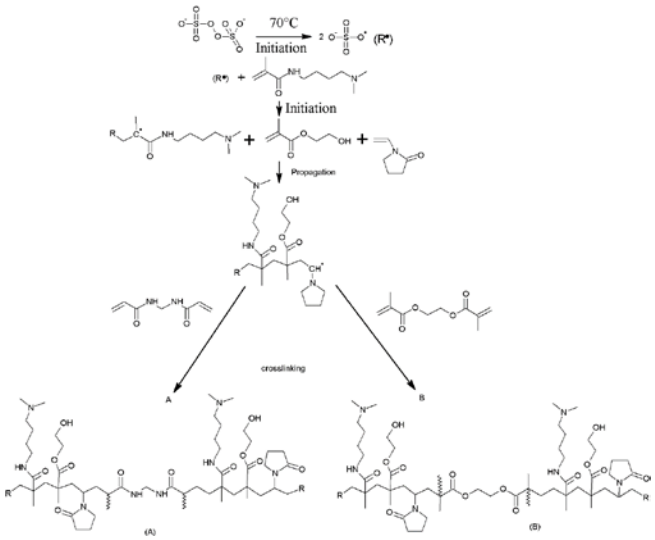
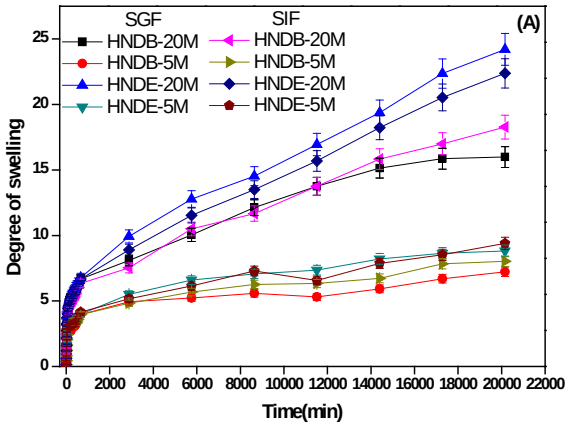


Fig. 3 Polymerization mechanism for the copolymers HNDB (A) and HNDE (B)



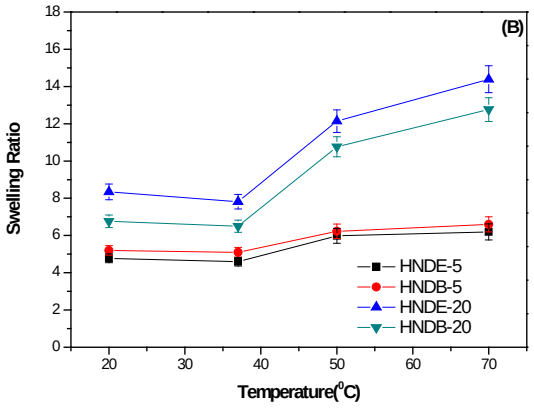


Fig. 4 A) Swelling of hydrogel in SGF and SIF at 37°C and B) swelling ratios of the hydrogels as a function of temperature in water

TG/DTG study

The TG/DTG traces of hydrogels formed using BMAA and EGDMA crosslinkers are shown in Fig. 7. BMAA crosslinked hydrogel showed a three step degradation. The weight loss at 70–120°C was due to the removal of moisture and other volatile impurities if any. The degradations in the temperature ranges 200-300°C and 300-350°C were attributed to the degradation of polymer backbones with olefinic chain ends and saturated aliphatic ends respectively. The thermal stability of polymer prepared with low mole% (0.0025%) of DMAPMA was greater than that for the one with high mole% (0.02%). For example with 0.02 and 0.0025 mole % of DMAPMA in the monomer feed, the residual weights at 475°C were 3% and 15% respectively. The same trend was observed with EGDMA crosslinked polymer hydrogel. This observation was also corroborated by the fact that at low mole% of DMAPMA the polymer obtained was comparatively less swellable. This may be attributed to the change in molecular weight of hydrogels due to DMAPMA catalyzed decomposition of potassium persulphate initiator[19] . This was also reflected in the residual weights observed at 475°C.

DSC study

The DSC traces of hydrogel and THP tablet displayed in Fig. 8 show multiple endotherms. The endotherms around 100°C in all the hydrogel samples were attributed to moisture loss. The endotherm at 310˚C in the HNDE-20 was more likely attributed to backbone degradation which was also revealed in TG (Fig.7) and this occurred roughly around 300˚C in the tablet. The marginal difference in the degradation temperatures may be due to polymer-THP physical interaction in the tablet.

XRD characterization

XRDs of the copolymers DHNB-2.5, DHNB-20, DHNE-2.5, and DHNE-20(Fig. 9) showed diffraction peaks at 2θ values 17.6, 17.9, 16.9 and 17.7 with peak intensities of 1283, 1737, 1318 and 1908 respectively. Comparison of these values implied that the copolymer derived from monomer feed having higher concentrations of DMAPMA possessed marginally higher diffraction peak intensity perhaps due to low molecular weight and hence less chain entanglement[20]. In general it can be projected that these copolymers seem to be predominantly amorphous in nature.

Cytotoxicity test

Usually the toxicity of the polymer hydrogel may be due to the trace amount of oligomer, unreacted monomer and other volatile impurities if any. Cell culture method can be used to evaluate the toxicity of hydrogels[11]. Cytotoxicity of the hydrogels was evaluated *in vitro* by direct and indirect methods, using NIH 3T3 fibroblasts as model cell line [21]. In the direct contact method, optical microscopic study revealed that cells possess normal morphology after 48-h incubation both with HNDE-20 (Fig. 10A) and HNDB-20 (Fig. 10B). A decrease of 20–25% was observed in the number of fibroblasts after exposure to the hydrogels. This may be attributed to the unreacted monomers trapped inside the hydrogel. Cell viability was tested by MTT colorimetric assay [22] (indirect method). Cell viability was assessed after exposing NIH3T3 cells to increasing concentrations of HNDE-20 and HNDB-20 hydrogels (31.25–500 µg/ml) (Fig.10(C &D)). Cytotoxicity studies through cell viability indicated a dose-dependent decrease pattern in fibroblast cell viability for HNDB-20 hydrogel. This was pronounced at a concentration of 500 µg/ml where the viability was 81.62%. For the polymer concentration range (31.25–62.5 µg/ml) a 11% reduction in cell viability was observed. But in HNDE-20 hydrogel for the concentration range (31.25–250 µg/ml) no significant reduction in cell viability was observed.

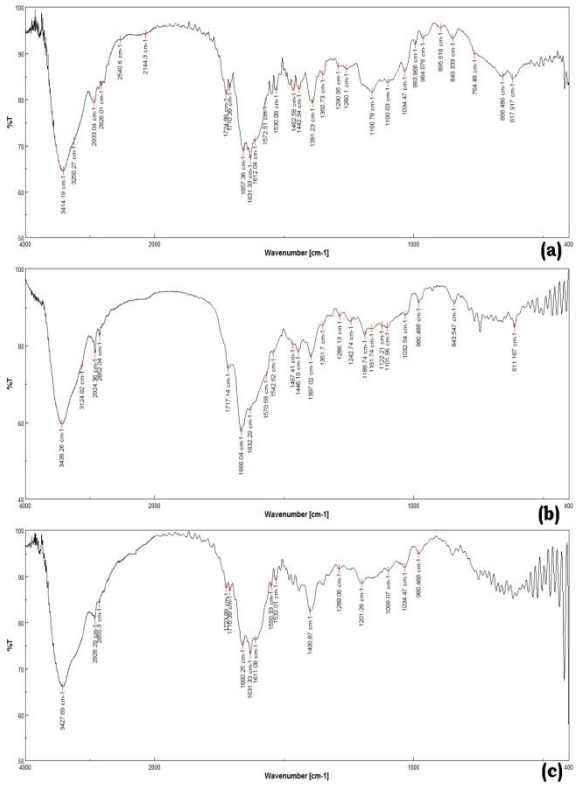


Fig. 5 FT-IR Spectra of HNDB (a), polymer-theophylline tablet before (b) and after (c) swelling in water

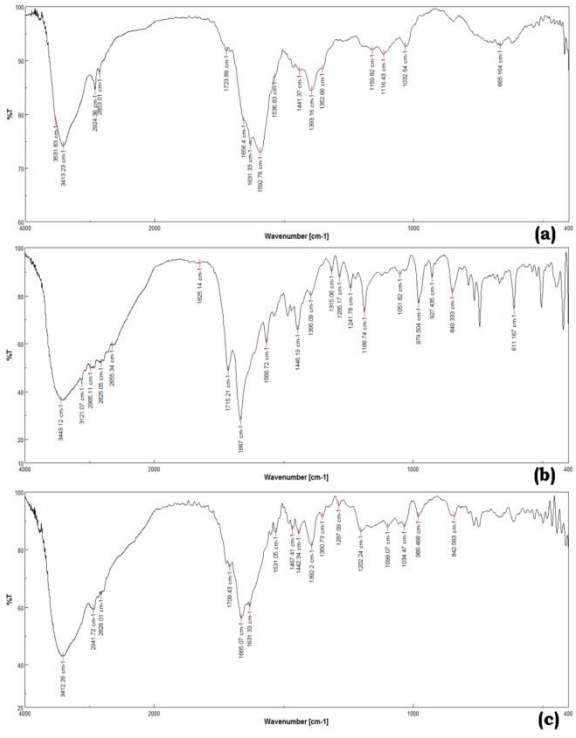


Fig. 6 FT-IR Spectra of HNDE (a), polymer-THP tablet before (b) and after (c) swelling in water

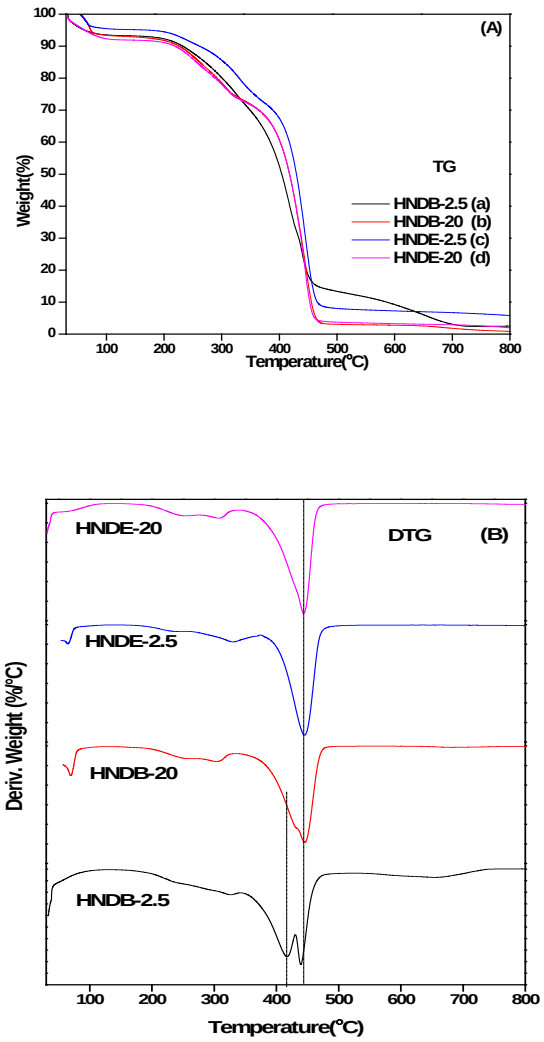


Fig. 7 TG (A) and DTG (B) traces of, (a) HNDB2.5, (b) HNDB20, (c) HNDE2.5 and (d) HNDE20

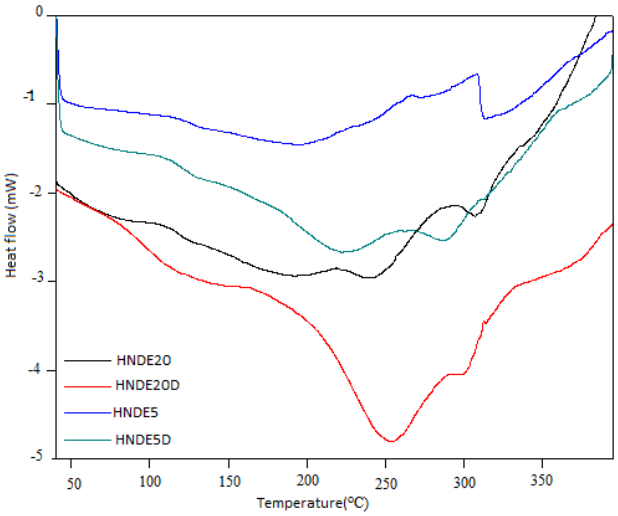


Fig. 8 DSC thermograms of (a) HNDE20, (b) HNDE20D, (c) HNDE5 and (d) HNDE5D

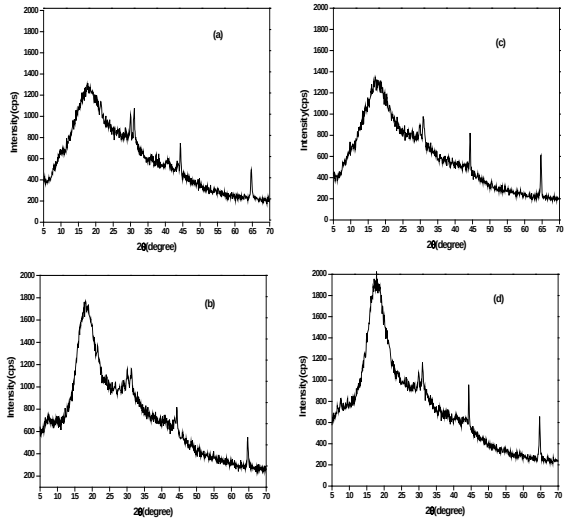


Fig. 9 XRD patterns of (a) HNDB2.5, (b) HNDB20, (c) HNDE2.5 and (d) HNDE 2.5

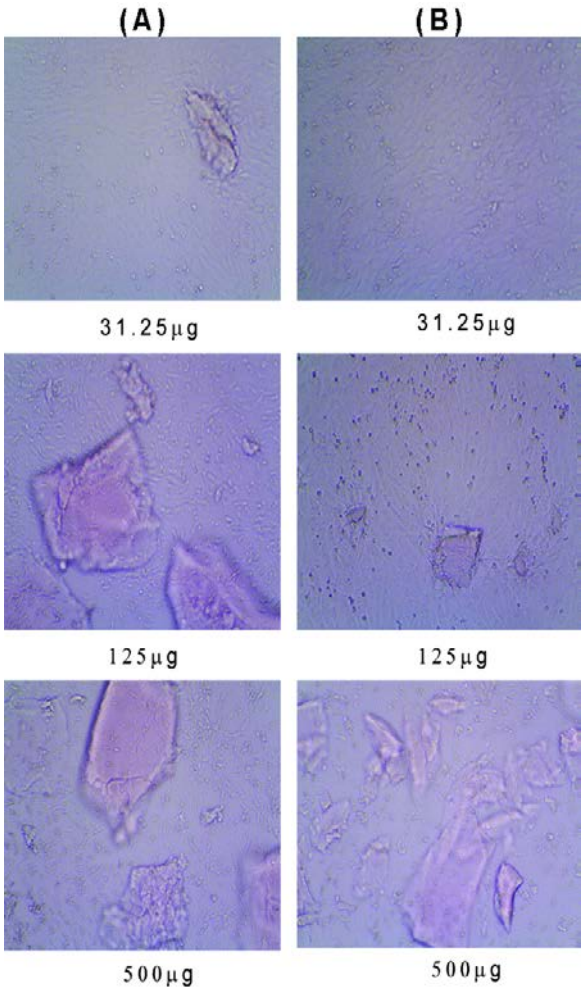


Fig. 10 (A&B) Optical microscopic photos of NIH 3T3 cell growth on HNDB20 (A) and HNDE20 (B)

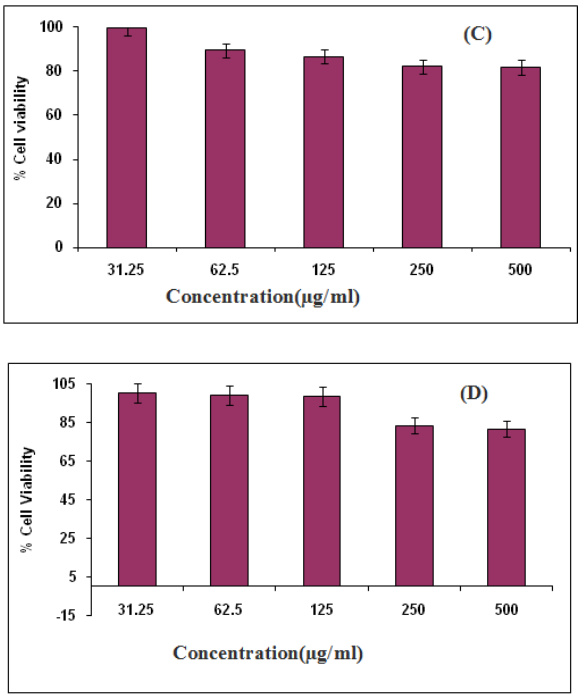


Fig. 10 (C&D) Histograms of % cell viability of NIH 3T3 cell for different concentrations concentrations of HNDB20(C) & HNDE20 (D)

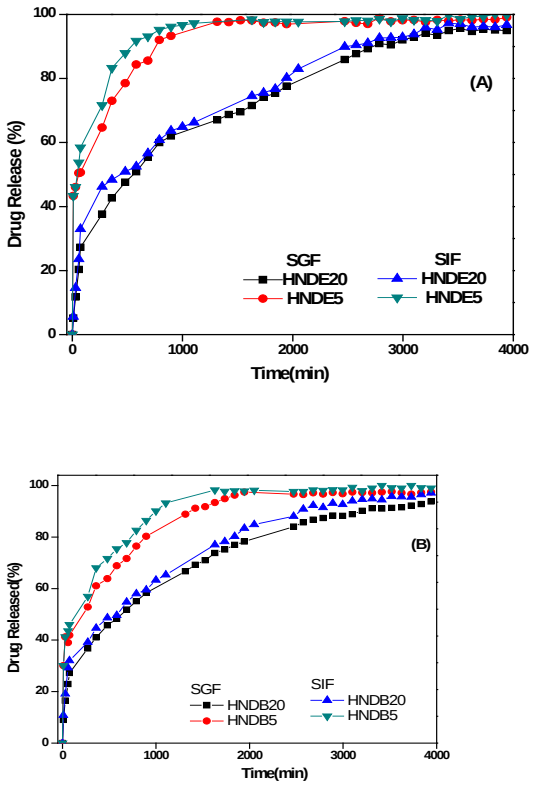
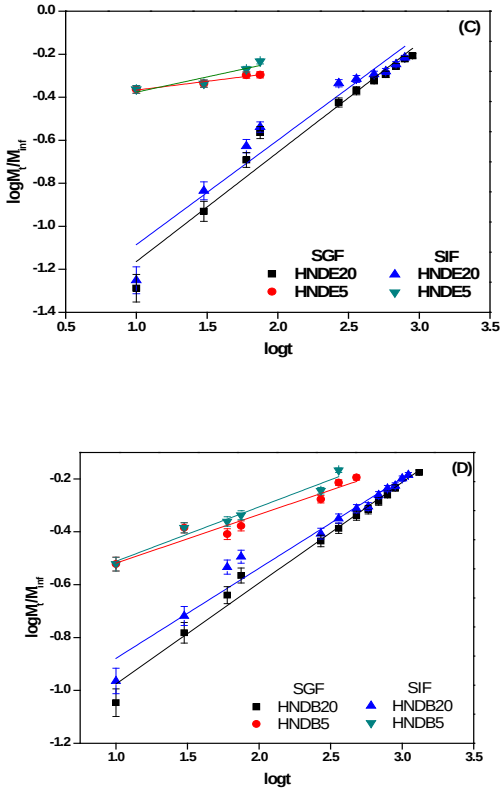


Fig. 11 Release profiles of THP in SGF and SIF for HNDE (A) and HNDB (B) carriers at 37°C



Figs.12 (C&D) Korsmeyer-Peppas plots for the release profiles of THP in SGF and SIF with HNDE (C) HNDB (D) carriers at 37°C

In vitro release study

The release profiles of THP from its tablet with HNDB and HNDE matrix in SGF and SIF are given in Fig. 11. There is not much difference in the drug release rate in SGF and SIF. For the carriers HNDE-20 and HNDB-20 the drug release rate upto 30% release was very high and then declined. > 95% drug release was observed beyond 60 h for both the cross linkers. For the carriers HNDE-5 and HNDB-5, > 95% drug release was observed within 17 hrs. The higher drug release rate for the low concentration of DMAPMA in the feed compared to that at high concentration may be attributed to the initial burst release due to the high rigidity of the tablet and low swellability of matrix in water, SGF and SIF. The drug release mechanism was analyzed using the power law equation [11]

$$M_t / M_\infty = kt^n \quad (4)$$

where M_t and M_∞ are the amounts of drug released at time‘t’ and at equilibrium, and ‘n’ and ‘k’ are the diffusion exponent and the proportionality constant characteristic of the drug–polymer system respectively. The initial drug release data as a function of the time for $0 \leq M_t / M_\infty \leq 0.5$ were fitted into the equation (4) (Fig.12) to estimate the release kinetic parameters. It was reported that release of drug via diffusion from the polymer matrix would follow a Fickian mechanism if n=0.5, an anomalous or non-Fickian type if n > 0.5 and a completely non-Fickian or Case II release kinetics[11] if n=1.0 . The ‘n’ values between 0.08 and 0.5for the pH 1.2 and 7.2 in the present

study suggested that the drug release mechanism appears to be either non-Fickian or Fickian depending on the composition of HNDB and HNDE polymer.

Computational study

The strength of a H- bond in a molecule is characterized by its bond dissociation energy as per equation 1. The strengths calculated for different types of H-bonds viz., >C=O----H-O, >C=O----H-N, >N----H-N<, >N----H-O- are summarized in Table 2. Analysis of the results in Table 2 indicated that the NC(O)N H-bonding interaction is more stable than that of NC(O)C by -12.19 kJ/mole and this difference was more likely due to the inductive effect (+I) of N-methyl groups in THP. Hence the DFT studies implied the existence of H- bonding interaction in the polymer-drug system. This may influence the THP release kinetics in water medium. The experimental data also suggested that H-bonding interaction in solid matrix is less compared to that in water medium.

Table 1 Composition of reactants in the polymerization recipe*

Polymer ID	Monomer/crosslinker/ initiator concentrations (mole/L)					
	DMAPMA	HEMA	NVP	BMAA	EGDMA	KPS
HNDB2.5M	0.25	0.5	0.5	0.00987	0	0.01849
HNDE2.5M	0.25	0.5	0.5	0	0.00987	0.01849
HNDB5M	0.5	0.5	0.5	0.00987	0	0.01849
HNDE5M	0.5	0.5	0.5	0	0.00987	0.01849
HNDB10M	1.0	0.5	0.5	0.00987	0	0.01849
HNDE10M	1.0	0.5	0.5	0	0.00987	0.01849
HNDB15M	1.5	0.5	0.5	0.00987	0	0.01849
HNDE15M	1.5	0.5	0.5	0	0.00987	0.01849
HNDB20M	2.0	0.5	0.5	0.00987	0	0.01849
HNDE20M	2.0	0.5	0.5	0	0.00987	0.01849
HNDB20MC	2.0	0.5	0.5	0.03205	0	0.01849
HNDE20MC	2.0	0.5	0.5	0	0.03205	0.01849

*Total volume of polymerization recipe: 10 ml

Table 2 Hydrogen bond dissociation energies

S.No	Type	Total Energy	ΔE	Dipole Moment
1	-N----H-N-DMAPAA	-2027.32103321	-44155.85	8.3946
2	-CN>C=O----H-N-DMAPAA	-2042.17386901	-5247.36	10.9088
3	-NN>C=O---- H-N-DMAPAA	-2043.32450376	-2233.16	12.2163
4	-N-H----O=C- DMAPAA	-2043.68743671	-1282.42	10.2078
5	-N-H----O=C-HEMA	-2043.89048454	-750.52	12.3552
6	-N-H----O-C-HEMA(ether)	-2044.00202483	-458.33	9.4805
7	-N-H----O-HEMA(hydroxyl)	-2044.01018319	-436.96	11.1634
8	-N-H----O=C-NVP	-2044.01341381	-428.49	13.7899
9	-N----H-O-HEMA	-2044.07729814	-261.14	7.0081
10	-N-H----N-NVP	-2044.08106213	-251.28	8.5490
11	-N-H----N-H DMAPAA	-2044.15084995	-68.47	11.2591
12	-NN>C=O----H-O-HEMA	-2044.17191323	-13.29	8.0189
13	-CN>C=O----H-O-HEMA	-2044.17655703	-1.12	9.8158
14	THP	-640.96527503	0	3.3486
15	Polymer	-1403.21171067	0	8.6698
16	-N-H----N-DMAPAA(terminal)	-2044.71909007	1420.10	11.9368

CONCLUSIONS

The crosslinked poly (DMAPMA-co-HEMA-co-NVP) hydrogels were synthesized, characterized and *in vitro* evaluated as drug carrier for controlled release of theophylline. Both the FT-IR spectrum of theophylline tablet and computational H-bond modeling indicated H- bonding interaction between polymer matrix and drug. This interaction which can be fine-tuned may contribute for the controlled release of drug. Swelling behavior of hydrogels in the temperature range 20-70°C showed that these hydrogels shrink in water at temperatures <35°C and swell at temperatures >35°C. This feature can be made use of for site specific delivery of drug. TG/DTG analysis revealed that thermal stability and swellability of hydrogel for low mole% (0.0025 %) of DMAPMA in monomer feed were greater and lower respectively than those with high mole % (0.02%), and these were due to the molecular weight effect. This was also supported by higher residual weight observed at 475°C in TGA for the polymer obtained using low mole % DMAPMA in the feed. XRD indicated that the polymer is predominantly amorphous. Cytotoxicity study of the polymer measured on the mouse embryonic fibroblast

NIH3T3 cells revealed that the polymer is cell viable. These observations convey that this hydrogel can be a promising thermoresponsive carrier for the controlled and targeted drug release of drugs by fine tuning its composition.

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