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Synthesis and characterization of Interpenetrating polymer network microspheres of acryl amide grafted Carboxymethylcellulose and Sodium alginate for controlled release of Triprolidine hydrochloride monohydrate

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ABSTRACT

Interpenetrating polymer network [IPN] microspheres of acrylamide (AAm) grafted on Carboxymethyl cellulose (CMC) and Sodium alginate (NaAlg) microspheres were prepared by water-in-oil (W/O) emulsion method. These microspheres were loaded with Triprolidine hydrochloride monohydrate (TPH) and cross-linked with glutaraldehyde. The prepared microspheres were characterized by Differential scanning calorimetry (DSC), Scanning electron microscopy (SEM) and Laser particle size analyzer. DSC thermo grams of TPH loaded AAm-g-CMC/NaAlg IPN microspheres confirmed the molecular level distribution in the polymer matrix. SEM of the microspheres suggested the formation of spherical particles. Swelling experiments on the microspheres provided important information on drug diffusion properties. Release data have been analyzed using an empirical equation to understand the nature of transport of drug containing solution through the polymeric matrices. The controlled release characteristic of the matrices for TPH was investigated in pH 7.4 media. Particle size and size distribution of the microspheres was studied by laser light diffraction particle size analyzer. Drug was released in a controlled manner upto 12 h.

INTRODUCTION

Interpenetrating polymeric networks (IPNs) have potential applications in the drug delivery and biomedical field. IPN has lead to the development of bioengineering tissues, such as bone substitutes, tissue, and cartilage scaffolds (Lim and Moss, 1981; Cai et al., 1989). Autologous tissue engineering provides an alternative for allogenic tissue transplantation. The study of IPN for drug delivery systems and tissue engineering may lead to a better understanding of critical diseases. The concepts of high swelling capacity, specificity, and sensitivity play a crucial role in targeting delivery of drugs. By understanding the nature of drug delivery systems and their durability in the body, which can interact with the systems, can be identified. IPN has various advantages as a biomaterial and is widely used as carrier systems for delivery of the short biological half-life drugs. There has been a spiky growth in the speed of discovery and development of IPN over the past few years. Current research supports the theory that IPN can provide the resources to deliver drugs at a prolonged controlled release to specific targets. Polysaccharides, a class of naturally available carbohydrate polymers, have been used extensively in food industry as gelling agents and for encapsulation of living cells, drugs etc (Ramesh Babu et al., 2007; Ueda et al., 1998; Palmieri et al., 1999). Among the systems for controlled release, prime attention has been paid in recent years to polymeric carriers (Loua et al., 2004) systems which may be natural (Yuk et al., 1995) or synthetic (Trimmnel et al., 1996) or combination of both the polymers (Gurdag et al., 1997). Natural polymers are biocompatible and biodegradable and some of the synthetic polymers are also biocompatible.

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Combination of these two types of polymers will enhance the properties of the matrix. One of the ways to increase the properties of natural (Shukla and Sharma, 1987; Nho and Jin, 1997; Celik and Sacak, 1996) and synthetic (Chan and Hang, 1998; Lim and Moss, 1981) polymers and to give them new properties is through graft copolymerization. Among the family of natural polysaccharides, Sodium alginate (NaAlg) is widely used for the preparation of drug delivery matrices viz., microspheres, membranes etc. NaAlg is water-soluble and it can be readily crosslinked with glutaraldehyde or Ca^{2+} ions. Alginate is a linear chain structure of (1-4)-linked β-D-mannuronic acid (M) and α-L-guluronic acid (G) residues arranged in a blockwise fashion. These blocks are constructed in three different ways: homopolymeric MM blocks, homopolymeric GG blocks and heteropolymeric sequentially alternating MG blocks (Hertzberg et al., 1995; Aminabhavi et al., 1999). The presence of α-L-guluronic acid in various ratios and molecular weight alters physico-chemical properties of the polymer (Lin and Ayres, 1992). This Polysaccharide has been used extensively in food industry as a gelling agent for encapsulation of living cells (Downs et al., 1992; Kumber and Aminabhavi, 2002; Cai et al., 1989).

Carboxymethylcellulose (CMC) is an important industrial polymer with a wide range of applications in flocculation, drag reduction, detergents, textiles, paper, food, drugs, and oil well drilling operation. CMC is a derivative of cellulose and formed by its reaction with sodium hydroxide and chloroacetic acid, it has a number of sodium carboxymethyl groups (CH_2COONa), introduced into the cellulose molecule, which promotes water solubility. Among all the polysaccharides, CMC is easily available and it is also very cheap. It has shear stability.

Polymers of acrylamide and its derivatives are well known for their hydrophilic and inert nature that makes them suitable for applications in medical and pharmacy. Polyacrylamide has been used in contact lenses for a long time and it has well been evaluated as a sustained release wound dressing material (Kulkarni et al., 2000). Fernandez et al. have evaluated the properties of glucose oxidase loaded polyacrylamide hydrogels to be used as glucose sensors (asghar et al., 2005) While Patton and Palmer, have reported hemoglobin and polyacrylamide based hydrogels as efficient oxygen carriers (Karadag et al., 1996). Polyacrylamide has also been extensively grafted onto natural and synthetic polymers like gelatin, carboxy methyl cellulose, poly ([gamma]-glutamic acid), Polyvinyl alcohol, collagen to obtain composite hydrogels with improved properties (Sommadossi et al., 1982; Korsmeyer and Peppas, 1981; Patel et al., 1994; Ritger and Peppas, 1987).

The synthetic polymers are much more effective than natural ones due to their versatile tailorability. However, they are not shear resistance. Several attempts have been made in the past to combine the best properties of both by grafting synthetic polymers onto natural ones. One of the great advantage thus obtained is the consequent reduced biodegradability because of the drastic change of the original structure of the natural polymer as well as the increased synthetic polymer content within the product. In the present work the authors have developed AAm-g-CMC/NaAlg blend microspheres for controlled drug release application by water-in-oil (W/O) emulsion method and loaded with TPH as a model drug. Controlled release capability and reducing toxicity of polymeric carriers are important for drug delivery applications. Triprolidine hydrochloride, chemically (ε) - 2-(3-pyrolidine-1-yl-1(4-toly) prop-1-enyl-pyridine hydrochloride monohydrate) (TPH), used as antihistamine with central sedative & antimuscrinic effect, for the symptomatic relief of hypersensitivity reaction including urticaria, skin disorders. The prepared microspheres have been characterized by FT-IR, X-RD, SEM and DSC techniques. In vitro released studies have been performed by dissolution experiments. Release data have been discussed in terms of fickian equation and diffusion parameters and the results are presented here.

EXPERIMENTAL

Materials

Carboxymethylcellulose (CMC), Acryl amide (AAm), Potassium persulphate, Glutaraldehyde (GA) solution 25% (V/V), Hydrochloric acid (HCl), n-hexane, Liquid paraffin oil (light) and Sodium alginate (NaAlg) were purchased from S. D. Fine Chemicals Ltd., Mumbai, India. Tween-80 was purchased from Aldrich., USA. Triprolidine hydrochloride monohydrate (TPH) drug was purchased from WaksmanSaleman Pvt. Ltd. Anantapur, India. Double-distilled water collected in the laboratory was used throughout this research work. All the chemicals were used as received without further purification.

Preparation of AAm-g-CMC/NaAlg TPH loaded IPN microspheres

Interpenetrating network (IPN), microspheres of acrylamide grafted on CMC and blended with Sodium alginate have been prepared by emulsion crosslinking method. In brief, known amount of CMC was dissolved in double-distilled water by continuous stirring until a homogeneous solution was obtained. To this solution different amounts of acryl amide and potassium per sulphate were added and stirred well to make a homogeneous solution. This reaction mixture is polymerized under nitrogen atmosphere for 6 h at 70°C. This polymerized AAm-g-CMC polymer product is cooled and precipitated in acetone and the precipitate was dried under vacuum for 24 h. A different weight ratio of Sodium alginate and AAm-g-CMC was dissolved in double-distilled water and stirred overnight until a homogeneous solution was obtained. A known amount of the Triprolidine hydrochloride monohydrate (TPH) was dissolved in 1 mL of double-distilled water and is added into the blend polymer solution.

The above drug loaded polymer solution was added slowly to a mixture of petroleum ether and light liquid paraffin (40:60, w/w) containing 1% (w/w) tween-80 under constant stirring at 300 rpm speed for 10 min. To this emulsion, 1 mL of

0.1 M HCl and GA was added slowly and further stirred for 30 min. This emulsion solution was filtered using Vacuum pump (High vacuum pump, Bangalore) and washed repeatedly with n-hexane and distilled water to remove the oil and excess amount of unreacted GA.

Microspheres thus formed were dried under vacuum at 40 ^{0}C for 24 h and stored in desiccator for further analysis and characterization. Repeating the above procedure various formulations were prepared by varying NaAlg, CMC, GA and TPH compositions and these are designated as NaAlg-1 to NaAlg-9 in **Table.1.**

Estimation of Drug Loading and Encapsulation Efficiency

Specific amounts of dry microspheres were vigorously stirred in a beaker containing 10 mL of dichloromethane to extract Triprolidine hydrochloride monohydrate from the IPN particles. A 10 mL of 7.4 pH phosphate buffer containing 0.02 % Tween-80 solution was added to the above solution, Triprolidine hydrochloride monohydrate was evaporated with a gentle heating and continuous shaking.

The aqueous solution was filtered and assayed by UV spectrophotometer (Lab India, Mumbai, India) at fixed λ_{max} value of 200 nm. The encapsulation efficiency is given with two digits with SD, which was measured by diffusion method i.e. the microspheres were dispersed in a buffer solution and made to swell. The release of drug into the buffer solution was measured spectrophotometrically. The results of % drug loading and encapsulation efficiency were calculated, respectively by using **Eqs: 1** and **2**.

$$\%\ \text{Drug loading} = \left(\frac{\text{Weight of drug in } \textit{microspher es}}{\text{Weight of microspher es}} \right) \text{x}\, 100$$

$$\%\ \textit{Encapsulat ion efficiency} = \left(\frac{\textit{Actual loading}}{\textit{Theoretica l loading}} \right) x\, 100$$

***In-vitro* Release Study**

In-vitro release studies have been carried out by performing the dissolution experiments using a tablet dissolution tester (Lab India, Mumbai, India). Dissolution rates were measured at 37 ± 0.5 ^{0}C at constant speed of 100 rpm. Drug release from the microspheres was studied in 0.1 M HCl and in 7.4 pH Phosphate buffer solutions. At regular intervals of time, sample aliquots were withdrawn and analyzed by UV spectrophotometer (Lab India, Mumbai, India) at the fixed λ_{max} value of 270 nm. After each collection, the same amount of fresh medium at the same temperature was added to the release medium to maintain the sink condition.

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectral measurements were performed with a Perkin Elmer, USA spectrophotometer. Polymeric microspheres were finely grinded with KBr to prepare pellets under a hydraulic pressure of 400 dynes/m^2 and spectra were scanned between 4000 and 400 cm^{-1}.

Differential Scanning Calorimetric (DSC) Studies

Differential Scanning Calorimetry (DSC) curves of the plain copolymer, plain TPH drug and drug loaded copolymer microspheres were recorded using a Rheometric Scientific differential scanning calorimeter (Model-DSC SP, UK).The analysis was performed by heating the samples at the rate of 10^{o}C/min under inert atmosphere.

X-Ray Diffraction (X-RD) Studies

The X-ray diffraction (X-RD) patterns of plain drug, plain microspheres and drug-loaded microspheres were recorded using a Rigaku Geigerflex diffractometer (Tokyo, Japan) equipped with Ni-filtered CuKα radiation (λ=1.5418A^o). The dried microspheres of uniform size were mounted on a sample holder and the patterns were recorded in the range 0 to 50^{0}C at the speed of 5^{0}C/min to know the crystallinity.

Particle Size and Scanning Electron Microscopic (SEM) studies

To determine the particle size and size distribution, ~ 100-200 microspheres were taken on a glace slide and their sizes were measured using an optical microscope under regular polarized light. Scanning electron microscope (SEM) micrographs of microspheres were obtained under high resolution (Mag 300 X 5kV) using JOEL MODEL JSM 840A, SEM, equipped with phoenix energy dispersive analysis of X-rays (EDAX).

RESULTS AND DISCUSSION

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR Spectra of AAm -g- CMC/NaAlg IPNM is depicted in Fig: 1. The spectra clearly marks the presence of amide group at 3420cm^{-1}(N-H stretching) and 1680 and 1660cm^{-1} (NH_2 bending), Carboxymethylcellulose unit bearing carboxylate ion at 1600 cm^{-1} strong asymmetrical stretching band and 1450 cm^{-1}(O-H bending of carboxylate ion). The most intense peak at 1557.4 cm^{-1} clearly indicates the crosslinking reaction between AAm -g- CMC , NaAlg and GA These values conforms the grafting of AAm on CMC.

Differential scanning Calorimetry (DSC) studies

DSC thermograms of pure TPH (Fig: 2. a), plain poly (AAm-g-CMC/NaAlg) microspheres, (Fig.2. b) and drug loaded poly (AAm-g-CMC/NaAlg) microspheres (Fig.2. c) are shown in Fig. 2. The drug, TPH, exhibit a sharp peak at 122.97 ^{0}C (Fig. 2. a) due to polymorphism and melting. However, no characteristic peak of TPH was observed in DSC curves of the plain microspheres in Fig. 2. b and drug-loaded microspheres in Fig. 2.c, suggesting that most of the drug was uniformly dispersed in polymer matrices at molecular level.

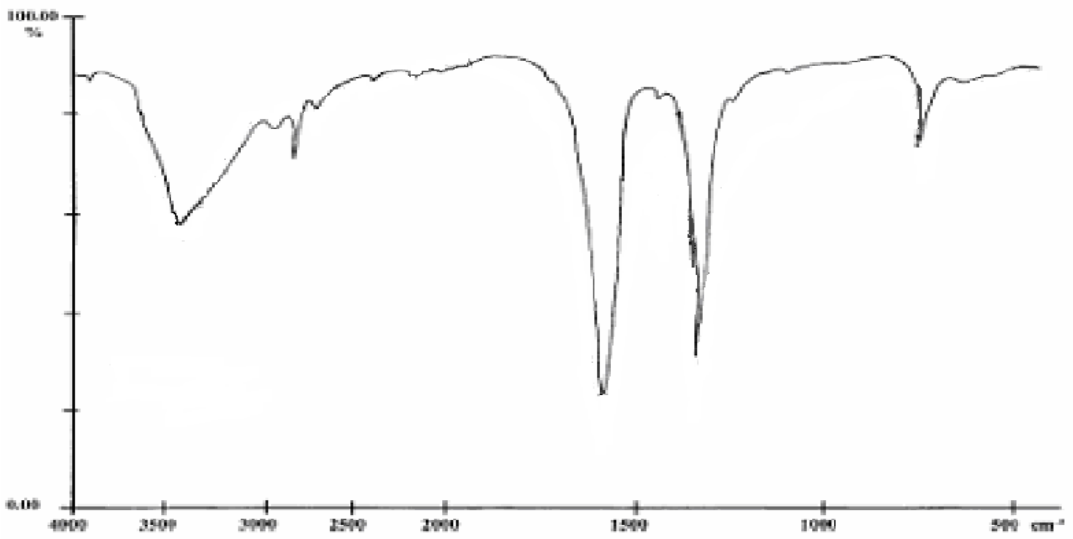

Fig: 1. IR spectrum of AAm -g- CMC/NaAlg.

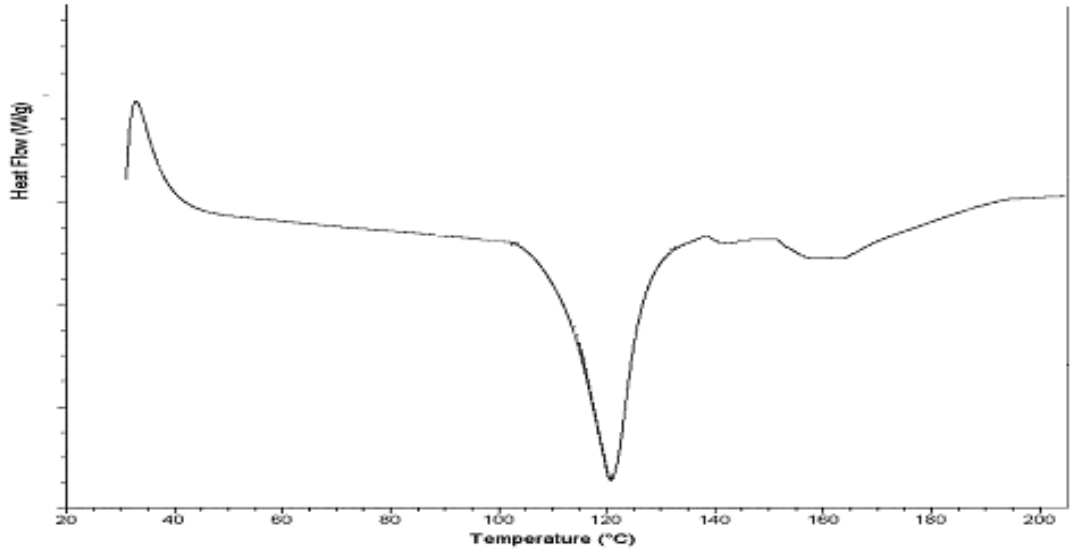

Fig. 2a: DSC thermograms of Triprolidine hydrochloride .

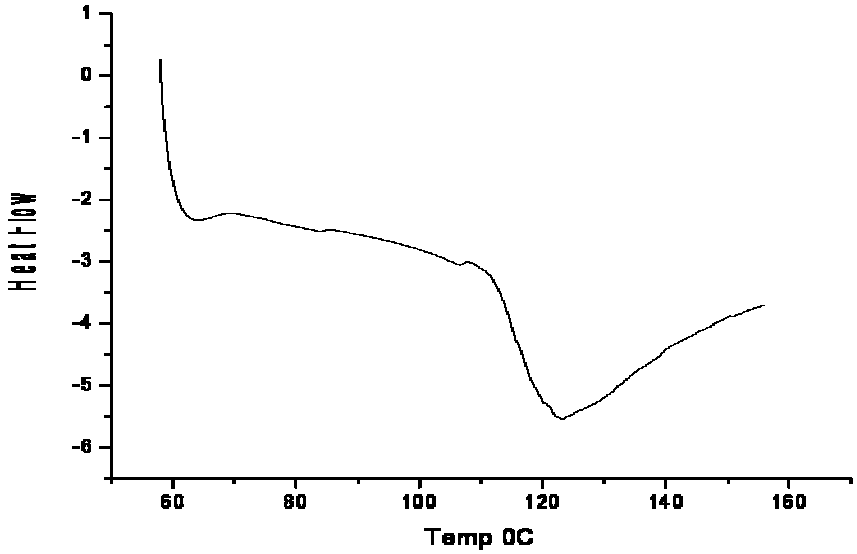

Fig. **2b:** DSC thermograms of plain AAm -g- CMC/NaAlg

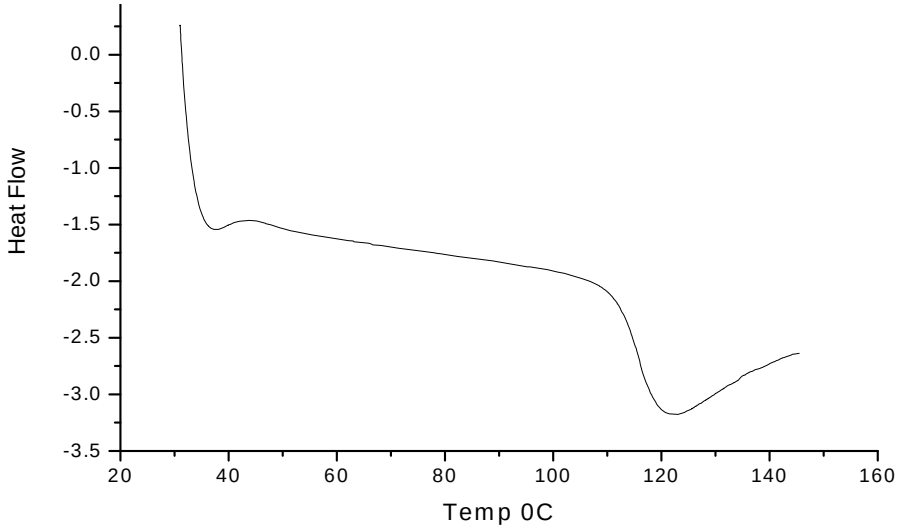

Fig. 2c: DSC thermograms of drug loaded AAm -g- CMC/NaAlg.

Scanning electron microscopic (SEM) studies

SEM images of the microspheres were recorded using a Hitachi S520 scanning electron microscope (Japan) at the required magnification. Working distance of 33.5 mm was maintained and the acceleration voltage used was 10 kV with the secondary electron image (SEI) as a detector. **Fig: 3.** Shows the SEM micrograph of tryprolininehydrochloride monohydrate loaded AAm-g-CMC/NaAlg microspheres, and they are spherical in nature.

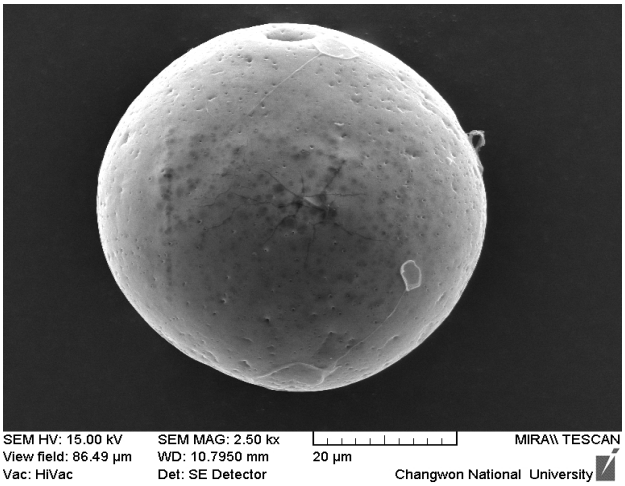

Fig. 3: Scanning electron micrograph of AAm-g-CMC/NaAlg microspheres.

Particle size analysis

Particle size and size distributions have been analyzed using a particle size analyzer (Mastersizer 2000, Malvern Instruments, UK). Results of mean diameter of the microspheres were obtained by taking three different amounts of crosslinking agent (NaAlg-1, NaAlg-2 and NaAlg-3 are 168,156,112 respectively.) and these values are presented in **Table. 1.** These results suggest that as the extent of crosslinking increases, the mean diameter decreases. On a population basis, particle size mean diameter decreases. On a population basis, particle size distribution is unimodel. Microspheres used in preparing drug-loaded formulations were selected from a uniform size distribution range as displayed in **Fig: 4**. A narrow size distribution of microspheres was observed with particle size 100-400 µm, but majorities of particles are in the range between 180-210 µm.

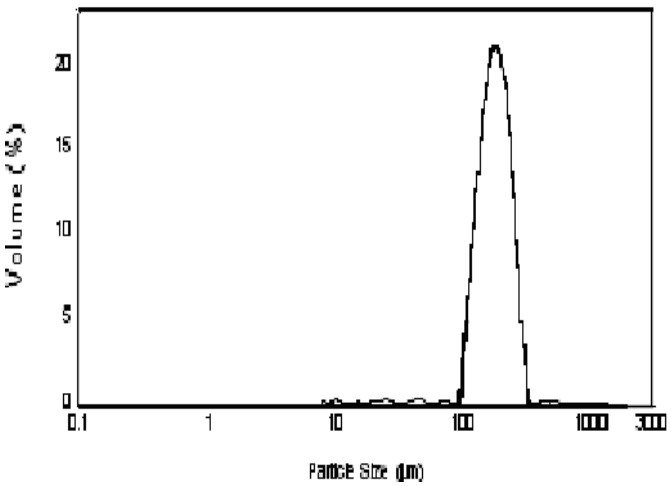

Fig. 4: Particle size distribution.

Estimation of drug loading and encapsulation efficiency

Specific amount of dry microspheres were vigorously stirred in a beaker containing 10 mL of dichloromethane to extract the drug from the microspheres.

A 10 mL of 7.4 pH phosphate buffer containing 0.02 % Tween-80 was added to the above solution to make the drug soluble and dichloromethane was evaporated with a gentle heating and continuous shaking. The aqueous solution was then filtered and assayed by a UV spectrophotometer (Lab India, Mumbai, India) at the fixed λmax value of 210nm. The results of encapsulation efficiency were calculated using **Eqs. 1** and **2.** And these results are compiled in **Table. 1.**

Table. 1: Results of % of encapsulation efficiency, mean particle size and water uptake of different formulations.

Formulation codes	Ratio of NaAlg: CMC in microspheres	Amount of AAm Added (mg)	Amount of TPH loaded (mg)	Amount of GA added (mL)	% Encapsulation efficiency ± S.D.	Mean particle size (μm) ± S.D.	% Water uptake
NaAlg-1	10:90	10	5	2.5	68.2 ± 0.8	168 ± 5	495
NaAlg-2	10:90	10	5	5	66.4 ± 1.1	156 ± 6	400
NaAlg-3	10:90	10	5	7.5	61.5 ± 0.9	112 ± 8	343
NaAlg-4	20:80	10	5	5	72.6 ± 0.8	160 ± 7	455
NaAlg-5	30:70	10	5	5	79.8 ± 1.2	175 ± 9	490
NaAlg-6	10:90	10	10	5	68.5 ± 1.1	168 ± 5	464
NaAlg-7	10:90	10	15	5	70.9 ± 1.5	155 ± 6	476
NaAlg-8	10:90	20	5	5	58.2 ± 0.4	185 ± 4	500
NaAlg-9	10:90	30	5	5	49.5 ± 0.6	208 ± 9	512

S.D: standard deviation

Swelling studies

Dynamic swelling of the AAm-g-CMC/NaAlg microspheres prepared using three different crosslink densities as well as three different drug loadings was studied in water by mass uptake measurements with time. Swelling experiments performed in 7.4 pH buffer solutions produced no significant changes and hence, we studied the swelling of microspheres in water [17]. To perform swelling experiments, microspheres were soaked in water, several of them were removed from the swelling bottles at different time intervals and blotted carefully with tissue paper (without pressing hard) to remove the surface-adhered water. The microspheres were then weighed (w_1) on an electronic microbalance (ADAM AFP-120 L accurate to ± 0.0001 g) and dried to a constant weight (w_2) in an oven maintained at 60^0C for 5 hours. Swelling experiments were repeated thrice for each sample and average values were used in data analysis. The standard deviations (S.D.) in all cases were < 5 %. The weight % water uptake was calculated using **Eq. 3**. Drug release rates are influenced by the equilibrium water up take of the cross linked microspheres (Ritger & Peppas, 1987). The % equilibrium water up take data of the cross liked microspheres presented in T**able. 1.** indicate that, as the amount of crosslinker (GA) in the polymer matrices increase from 2.5 to 7.5 mL, equilibrium water up take decreases significantly from 495, 400 & 343 (NaAlg-1, NaAlg-2 & NaAlg-3)respectively. The reduction in water up take may be due to the formation of a rigid net work structure at higher extent of crosslinking. It is also noted that formulations containing higher amount of AAm-g-CMC (NaAlg-5) showed higher swelling rates than those formulation containing lesser amount of AAm-g-CMC (NaAlg-4). This is attributed to the extremely hydrophilic nature of AAm-g-CMC/NaAlg polymer matrix, leading to higher water up take.

Drug release kinetics

Drug release kinetics was analyzed by plotting cumulative release data vs time and by fitting these data to the exponential equation of the type [27].

Here, M_t/M_∞ represents the fractional drug released at time *t, k* is a constant characteristic of the drug-polymer system and *n* is an empirical parameter characterizing the release mechanism. Using the least squares procedure, we have estimated the values of *n* and *k* for all the nine formulations and these values are given in **Table. 2**. If $n = 0.5$, the drug diffuses and releases from the polymer matrix following a Fickian diffusion. For $n > 0.5$, anomalous or non-Fickian type drug diffusion occurs. If $n = 1$, a completely non-Fickian or Case II release kinetics is operative. The intermediary values ranging between 0.5-1.0 are attributed to the anomalous type transport.

$$\left(\frac{M_t}{M_\infty} \right) = kt^n \quad \textbf{(4)}$$

The values of *k* and *n* have shown a dependence on the extent of crosslinking, % drug loading and AAm content of the matrix. Values of *n* for microspheres prepared by varying the amount of NaAlg in the polymer microspheres of 10, 20 and 30 % by keeping TPH (5 %) and GA (5 mL GA) constant, ranged from 0.206 to 0.680 leading to a shift of transport from Fickian to anomalous type. The TPH -loaded particles have the *n* values ranging from 0.195 to 0.540 **(Table. 2)**, indicating the shift from errosion type release to a swelling-controlled, non-Fickian mechanism. This could be possibly due to a reduction in the regions of low microviscosity and closure of microcavities in the swollen state. Similar findings have been observed elsewhere, wherein the effect of different polymer ratios on dissolution kinetics was studied. On the other hand, the values of *k* are quite smaller for the drug-loaded microspheres, suggesting their lesser interactions compared to microspheres containing varying amount of Sodium alginate.

Table . 2: Release kinetics parameters of different formulations.

Formulation codes	K	n
NaAlg-1	0.153	0.540
NaAlg-2	0.206	0.206
NaAlg-3	0.239	0.195
NaAlg-4	0.111	0.215
NaAlg-5	0.154	0.680
NaAlg-6	0.239	0.239
NaAlg-7	0.385	0.385
NaAlg-8	0.156	0.298
NaAlg-9	0.919	0.334

Effect of Acrylamide

Fig: 5. Shows the in vitro release data of TPH from the microspheres particles performed with different ratio of AAm in the polymeric particles. The data shows that higher amount of

AAm containing particles have more encapsulation efficiency and also the release studies show that higher amount of AAm containing particles have shown prolonged release characteristics than the microspheres containing lower amount of AAm. Generally, the drug release pattern depends on many factors like particle size, crystallinity, surface character, molecular weight, polymer composition, swelling ratio, degradation rate, drug binding affinity and the rate of hydration of the polymeric materials, etc. In the release behavior of polymeric system we can consider the binding affinity of drug and polymer swelling property of AAm. A rapid release of more than 98% of drug was observed within 12 h. by the microspheres containing lower amount of AAm indicating the interaction between the two polymers.

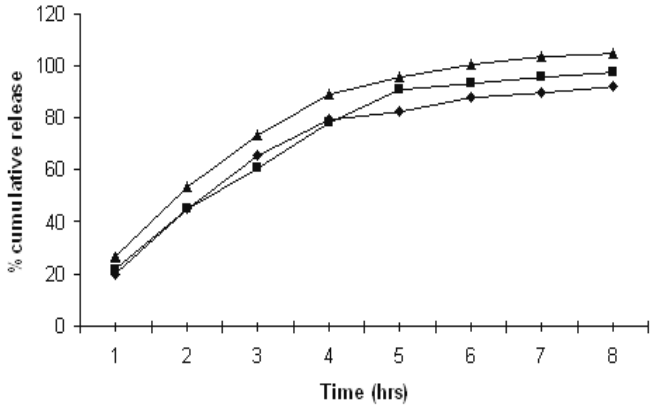

Fig. 5: % Cumulative release of TPH through AAm–g-CMC/ NaAlg Microspheres containing different amount of AAm. Symbols: (♦) 10 wt. %AAm (■) 20 wt. % AAm (Δ) 30 wt. %.

Effect of crosslinking agent

The % cumulative release data vs. time plots for varying amounts of GA i.e., 2.5, 5.0 and 7.5 mL at the fixed amount of the drug (5 %) are displayed in **Fig: 6.** The % cumulative release is quite fast and large at the lower amount of GA (i.e., 2.5 mL), whereas the release is quite slower at higher amount of GA (i.e., 7.5 mL). The cumulative release is somewhat smaller when lower amount of GA was used probably because at higher concentration of GA, polymeric chains become rigid due to the contraction of microvoids, thus decreasing % cumulative release of TPH through the polymeric matrices. As expected, the release becomes slower at higher amount of GA, but becomes faster at lower amount of GA.

Effect of percent drug loading

Fig: 7. Shows the release profiles of TPH loaded AAm-g-CMC/NaAlg microspheres at different amount of drug loadings. Release data showed that formulations containing the highest amount of drug (15 %) displayed fast and higher release rates than those formulations containing a small amount of TPH. A prolonged release was observed for the formulation containing lower amount of TPH. In other word, with decreasing amount of drug in the matrix. Due to the availability of more free void spaces through which lesser number of drug molecules will transport. For all the TPH -loaded formulations, the complete release of TPH was not observed even after 600 min, but the release rates were around 700 min.

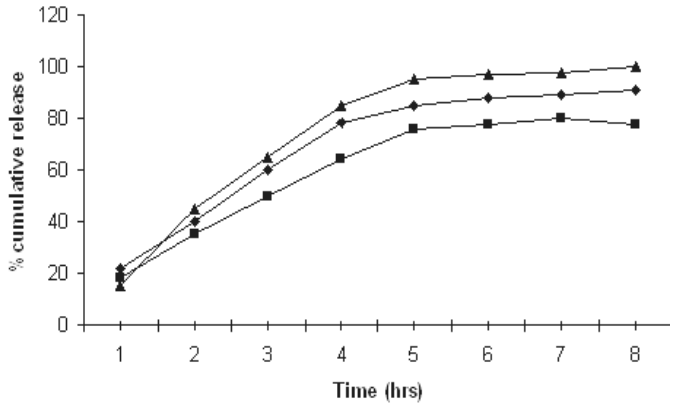

Fig. 6: % Cumulative release of TPH through AAm–g-CMC /NaAlg microspheres containing different amount of crosslinker. Symbols: (Δ) 2.5mL, (◊) 5mL (■) 7.5mL.

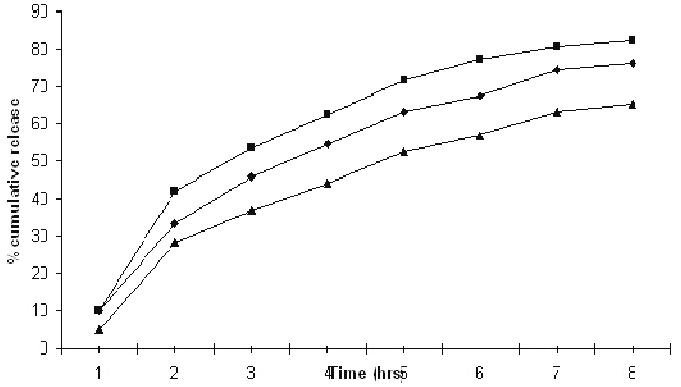

Fig. 7: % Cumulative release of TPH through AAm–g-CMC /NaAlg microspheres containing different amount of TPH. Symbols: (◊) 10 wt. %(Δ) 20 wt. % (■) 30 wt. %

Effect of percent sodium alginate content

Effect of NaAlg content was studied at constant loading of drug. The release trends of AAm-g-CMC / NaAlg microspheres prepared with different amounts of NaAlg are displayed in **Fig: 8.** Notice that during dissolution experiments, the microspheres have shown systematic swollen trends with decreasing amount of NaAlg probably due to the formation of loosely crosslinked net work chains of NaAlg.

As the amount of NaAlg increases, cumulative release decreased due to lesser swelling of the NaAlg chains than CMC. This could be because as the amount of NaAlg increases in semi-IPN matrix, the hydrophobicity of the overall matrix increases, there by decreasing the release rate for drug. Thus, a regaining – type response of polymeric chains is possible due to the stresses induced by the surrounding solvent media during the dissolution step, resulting in decrease of chain dimension (radius of gyration) of the semi-IPN polymer, this will further decrease the molecular volume of the hydrated polymer due to decreased swelling of NaAlg component of the semi-IPN matrix, there by reducing the free volume spaces of the matrix.

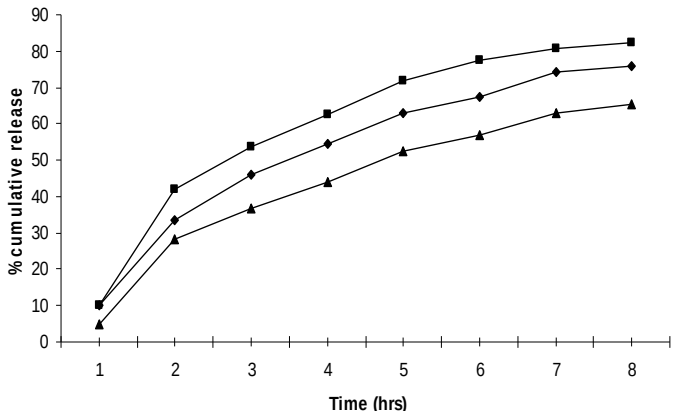

Fig. 8: % Cumulative release through AAm–g-CMC /NaAlg microspheres Containing different amount of NaAlg Symbols: (◊) 10 wt. % (■) 20 wt. % (Δ) 30 wt. %

CONCLUSIONS

Carbohydrate polymeric microspheres consisting of acrylamide grafted on carboxymethylcellulose and blended with sodium alginate were prepared and characterized by differential scanning calorimetry, scanning electron microscopy and particle size analyzer. DSC thermograms show the molecular distribution of drug in the microspheres and SEM micrographs show the spherical morphology of the prepared microspheres. The drug has been release in a controlled manner.

The swelling studies of the microspheres show that with the increasing amount of sodium alginate in the microspheres, the water uptake has increased and it is correlated with the sodiumalginate release of drug though the microspheres containing different amount of sodiumalginate. The microspheres have lower densities and hence, could be retained in gastric environment for more than 12 h, which might help to improve the bioavailability of TPH.

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