# Effect of Coexcipients on Drug Release and Floating Property of Nifedipine Hollow Microspheres: A Novel Gastro Retentive Drug Delivery System

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**ABSTRACT:** A gastro retentive drug-delivery system for nifedipine was developed by incorporating the drug in cellulose acetate hollow microspheres capable of floating on the gastric and intestinal fluid. The microspheres were prepared by solvent diffusion–evaporation technique in the presence of coexcipients like polyethylene glycol, dibutyl phthalate, and poly(ε-caprolactone) using ethyl acetate as a dispersing solvent. Size of the microparticles depends upon the type and concentration of the excipient used. Microparticles exhibited floating properties on the simulated-gastric fluid for >12 h. Their percentage buoyancy followed the rank order of: blank (no coexcipients) > dibutyl phthalate > polyethylene glycol > poly(ε-caprolactone) after 15 h of floating. Release of nifedepine was enhanced by the addition of coexcipients. The drug release followed non-Fickian transport in almost all formulations. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 100: 486–494, 2006

**Key words:** drug-delivery systems; floating hollow microspheres; excipients; nifedipine; non-Fickian transport

## INTRODUCTION

The variability of gastric emptying will make the in vivo performance of the oral drug-delivery system unpredictable.[1] Various attempts have been made to prolong the gastric retention time (GRT) of the dosage form, thereby, to increase the delivery time for >12 h, which otherwise would be restricted to 8–12 h when administered orally. One such method is the preparation of a device that remains buoyant in the stomach because of its lower density than that of the gastric fluid; these floating drug-delivery systems are also called hydrodynamically controlled release systems. Of the many approaches developed, the single unit dosage forms are of major interest. However, these systems have the disadvantages of all-or-none emptying process.[2] Efforts have been made in the literature[3–6] to develop oral floating mulitiparticulate drug-delivery systems for specific applications to optimize the dosage form. We have previously reported preparation of novel microspheres by solvent diffusion–evaporation method.[7] Drug release depends upon the inherent properties of the polymer, physicochemical properties of the drug, geometry or type of the delivery system. However, release kinetics and physicochemical properties can be manipulated by incorporating the plasticizers,[8] channeling agents,[9] and by using low-molecular weight polymers. In the present study, we report the effect of some coexcipients on floating and release properties of hollow microspheres.

In the present study, a new protocol has been developed to produce floating hollow microspheres of cellulose acetate (CA). The effect of coexcipients, like polyethylene glycol-400 (PEG), dibutyl phthalate (DBP), and low-molecular-weight poly(ε-caprolactone) (PCL), has been investigated on their release characteristics for nifedefine (NFD), a water-insoluble antihypertensive drug. The size, shape, buoyancy, and thermal behavior of the hollow microspheres have been studied. Microspheres were free flowing and floating for >12 h, and hence, drug release was controlled for >10 h.

## EXPERIMENTAL

### Materials

CA (received as a gift sample from Gujarat State Fertilizers Corp., Vadodara, India), PCL (intrinsic viscosity, 16.18 dL/g) (Sigma Aldrich, USA), PEG, DBP,

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ethyl acetate, acetone, chloroform, poly(vinyl alcohol) (MW: 125,000), sodium lauryl sulfate (SLS), polysorbate-80 (s.d. fine Chemicals, Mumbai, India) and nifedipine (received as gift sample from Lincoln Pharmaceuticals, Ahmedabad, India) were used in this research. All other reagents were of analytical grade and used without further purification.

### Preparation of hollow microspheres

Microspheres of CA were prepared by the modified procedure reported earlier.[7] Briefly, 100 mg of CA is dissolved in a mixture of 95-mL ethyl acetate and 5 mL of acetone in a cold-water bath. To prepare the CA–PCL blend microspheres in different compositions (10, 20, and 50%), PCL was dissolved separately in 4-mL chloroform and then added to the CA solution prepared earlier. The concentration of PCL used in microspheres was 10% (CA–PCL-1), 20% (CA–PCL-2), and 50% (CA–PCL-3) keeping the total volume of the polymer solution as 50 mL.

Microspheres of PEG and DBP were prepared by using different concentrations of plasticizers viz., DBP 10% w/w (CA–DBP-1), 20% w/w (CA–DBP-2), 40% w/w (CA–DBP-3) and PEG 10% w/w (CA–PEG-1), 20% w/w (CA–PEG-2), 40% w/w (CA-PEG-3) based on the dry mass of CA. NFD 10% w/w (based on the dry mass of CA) was dissolved in the polymer solution. The resulting solution was added slowly over a period of 1 min to 150 mL of 0.05% (w/v) aqueous poly(vinyl alcohol) (PVA) solution. The emulsion was continuously stirred at 500 rpm using Eurostar (IKA Labortechnik, Staufen, Germany), at room temperature. After 1 h, the partially hardened floating microspheres were decanted to 100 mL of water and stirred magnetically for 4–5 h.

The percentage hydration (i.e., mass percent of water uptake) of the microspheres was obtained gravimetrically. A small sample of the microspheres was taken, surface-adhered water droplets were wiped off with the help of a soft tissue paper, and mass ($W_1$) was taken on a digital microbalance (Mettler, AT20, Switzerland) within an accuracy of $\pm 0.01$ mg. Microspheres were then dried to a constant mass ($W_2$). Using these data, the percentage hydration was calculated as

$$\% \text{ Hydration} = [(W_1 - W_2)/W_2] \times 100 \qquad (1)$$

The floating microspheres were then collected and dried at 40°C in an oven. The microspheres were then stored in a desiccator until further use. Blank formulation was prepared as earlier without any coexcipients.

### Characterization of hollow microspheres

Microspheres were characterized for micromeritic properties like particle size, tapped density, compressibility index, true density, and flow property. The particle size was measured using an optical microscope under regular polarized light, and the mean particle size was calculated by taking 200–300 particles using the calibrated ocular micrometer.

The density of hollow microspheres was determined by immersing them in 0.02% Tween-80 solution for 3 days in a metal mesh basket. The microspheres that were sunk after this process are used for density measurement by the displacement method.

The angle of repose, $\phi$ of the microspheres, which measures the resistance to particle flow, was calculated as[10]

$$\tan \phi = 2H/D \qquad (2)$$

where 2 *H/D* is the surface area of the free-standing height of the microspheres' heap formed after making the microspheres flow from the angle funnel.

Fourier transform infrared (FTIR) spectra were obtained to investigate the possible interactions between polymer/coexcipients and NFD. Scanning electron microscopy (SEM) (JSM 6400, Nihon Denshi Co., Japan) was used to investigate the surface morphology of the microspheres. Differential scanning calorimetric (DSC) analyses were performed using a DuPont-2000 microcalorimeter (USA). Samples were continuously heated at the heating rate of 10°C/min under a constant flow of nitrogen gas.

### In vitro floating experiments

Floating microspheres were spread on a 100 mL of simulated gastric fluid (0.1*N* HCl) containing 0.02% w/v of polysorbate-80. The solution was stirred at the speed of 100 rpm at 37°C, using the multiple-point stirrer. After specific intervals of time, the fractions of microspheres (floating as well as the settled microspheres) were collected to calculate percentage buoyancy using the equation[11]

$$\% \text{ Buoyancy} = [Q_f/(Q_f + Q_s)] \times 100 \qquad (3)$$

where, $Q_f$ and $Q_s$ are masses of the floating and settled the hollow microspheres, respectively.

### In vitro drug release experiments

Drug release from the hollow microspheres is somewhat complicated, since the particles float and adhere on the inside surface of the dissolution baskets during the dissolution experiments. This would pose some problems in releasing NFD from the microsheres. To avoid this problem, we have used the standard USP peddle method, wherein microspheres were placed in a nonreacting mesh, having smaller mesh size than the microspheres. The mesh was tied with a nylon thread

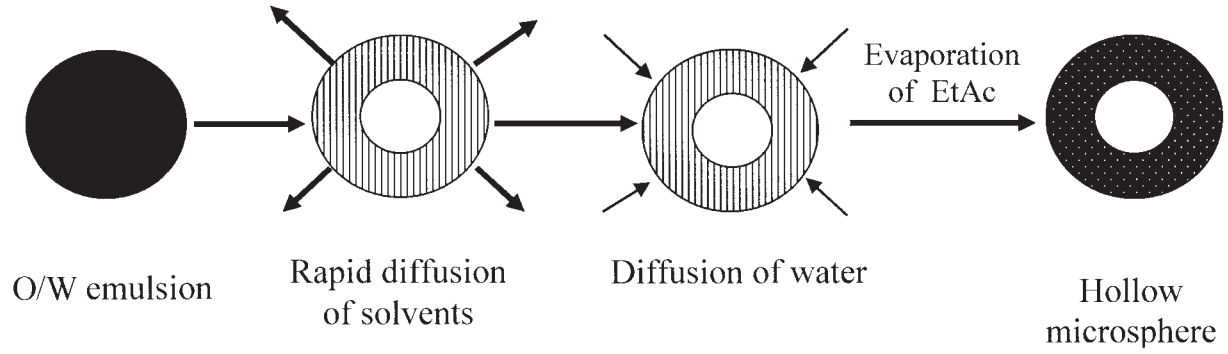


**Figure 1** Mechanism of the formation of hollow microspheres.

to avoid the escape of any microspheres. The glass marble was used in the mesh to help induce sinking of the microspheres in the dissolution medium viz., 900 mL of 0.1*N* HCl containing 0.1% SLS. Sample aliquots (10-mL) were withdrawn and analyzed at specific time intervals. Amount of NFD was then estimated using the UV–vis spectrophotometer (Secomam, Model Anthelie, France) at the $\lambda_{max}$ value of 238 nm.

## RESULTS AND DISCUSSION

### Physicochemical characteristics

A number of different methods have been used in the literature to produce the drug-loaded hollow microspheres.[3] While many physicochemical parameters are important in producing such floating/hollow microspheres, the main problem is to create a hollow space. To achieve this, we have used the solvent diffusion and evaporation technique, using a less-toxic ethyl acetate solvent. The mechanism of formation of hollow structure is depicted schematically in Figure 1. In a recent study by Joseph et al.,[6] a similar observation was made on piroxicam-loaded polycarbonate microspheres prepared by solvent evaporation method. The particles prepared were spherical in shape, but some were elongated.

To tailor the hollow microspheres, parameters like oil/water ratio, stirring speed, microsphere recovery, and drying techniques were carefully controlled. While pouring the polymer solution into an aqueous phase, an oil/water (o/w) emulsion with a phase ratio of 1:3 is created, since all the acetone might diffuse outside the cavity along with a small amount of ethyl acetate. Such a sudden diffusion of organic solvents into aqueous phase will induce an interfacial polymer deposition at the inner surface of the microspheres forming the hollow structure.[12,13] The aqueous phase might also diffuse in the hollow space, because the solubility of water in ethyl acetate is 3.65 v/v%, and thus, water might act as a poor solvent for the polymer, thereby, leading to polymer precipitation creating a hollow core in the CA microspheres.

Coexcipients like plasticizers polymers, and channeling agents are used in the polymeric matrix to manipulate the release profiles of the drug and also, the physicochemical properties of the matrix. In this study, we have extended our research to incorporate few coexcipients at different concentrations and studied their effect on properties like yield, drug-release kinetics, and buoyancy of the hollow microspheres. In almost all formulations, we have obtained the hollow/floating microspheres. The coexcipients influenced the yields of the final products (yield of hollow/floating microspheres). For instance, in case of CA + PCL formulations with 10% PCL, 82% yield was obtained (see Table I). On further increasing the PCL content, the yield was reduced to 37%. Such a drastic decrease in yield is due to a decrease in the concentration of CA for precipitation to occur at o/w interface during rapid diffusion of ethyl acetate. The PCL may not participate in this process, but might have remained in the hollow portion of the microspheres along with dichloromethane (DCM), which is relatively a good solvent for PCL. Thus, CA plays an important role in the formation of a hollow cavity. When the microspheres are plasticized with PEG or DBP, higher yields were obtained. Thus, for CA–PEG formulations, the yields varied from 75 to 86%, while for CA–DBP formulations, yields ranged between 71 and 72%. The latter values are quite close to the yield (70%) observed for blank microspheres.

Water uptake or extent of hydration of polymeric systems could dictate the transport of drug or drug release. The coexcepients in polymeric matrices could also influence the rate and extent of water uptake. However, in the case of floating devices, water uptake will influence their buoyancy. Hydration depends upon the nature of the excipient used. For instance, with PEG-containing microspheres, the percentage hydration is exceedingly higher (308–620%) than other microspheres; however, the (excipient-free)

**TABLE I**
**Effect of Coexcipients on Physicochemical Properties of Drug-Loaded Hollow Microspheres**

| Formulation code | Yield[a] (%) | Size ($\mu$m) | Hydration (%) | Buoyancy[b] (%) | $\phi$ (°) | Encapsulation efficiency (%) |
|---|---|---|---|---|---|---|
| CA–PCL-1 | 82.12 | 318 | 137 ± 19 | 26.1 ± 2.1 | 28.12 | 91.9 ± 4.0 |
| CA–PCL-2 | 46.43 | 264 | 268 ± 17 | 17.3 ± 3.2 | 27.47 | 82.4 ± 3.4 |
| CA–PCL-3 | 37.43 | 268 | 104 ± 10 | 5.8 ± 2.3 | 37.95 | 91.8 ± 5.1 |
| CA–PEG-1 | 75.55 | 584 | 308 ± 24 | 51.3 ± 9.1 | 27.47 | 71.1 ± 4.1 |
| CA–PEG-2 | 86.88 | 488 | 443 ± 21 | 24.9 ± 2.1 | 29.68 | 72.5 ± 3.3 |
| CA–PEG-3 | 83.58 | 585 | 620 ± 29 | 11.8 ± 5.4 | 26.10 | 83.2 ± 9.0 |
| CA–DBP-1 | 72.72 | 499 | 78 ± 10 | 82.1 ± 3.8 | 33.02 | 85.9 ± 6.7 |
| CA–DBP-2 | 72.22 | 396 | 95 ± 8 | 60.8 ± 7.1 | 26.10 | 83.0 ± 3.8 |
| CA–DBP-3 | 71.19 | 439 | 104 ± 15 | 68.1 ± 5.5 | 25.64 | 81.1 ± 5.3 |
| Blank | 70.66 | 549 | 216 ± 28 | 82.3 ± 10.1 | 27.20 | 95.9 ± 4.2 |

[a] [Mass of hollow microspheres/(mass of polymer + mass of drug)] × 100.
[b] Values after 15 h.

blank microspheres have a hydration of 216%, which increases considerably by increasing the amount of PEG. This is because PEG imparts higher hydrophilicity to the microspheres and thus, increasing their hydrating power. On the other hand, DBP-containing microspheres have much lower values of hydration (78–104%), but only a marginal increase is observed with increasing concentration of DBP. These values are much smaller than those observed for other PEG-containing formulations due to the hydrophobic nature of DBP. Ram Rao and Diwan[9] reported higher water vapor permeability for PEG-600-plasticized-CA films when compared to DBP-plasticized films. The PCL-containing microspheres have shown quite irregular trends for percentage hydration ranging between 104 and 268.

### Size and morphology of the microspheres

The NFD-loaded CA microspheres are predominantly spherical in appearance, even though some are elongated. The particles floated on both simulated gastric and intestinal fluids. Size (549-$\mu$m) of the blank microspheres is higher than that of the drug-loaded microspheres. The sizes (264–318 $\mu$m) of CA–PCL formulations are smaller than other formulations. The higher size ranges between 488 and 585 $\mu$m are observed for CA–PEG formulations. As partially hardened microspheres are resuspended in 100-mL fresh distilled water for quick drying to avoid the slow leaching of ethyl acetate and subsequent inward shrinkage of the matrix giving larger a size.[13,14] After adding PEG or DBP, the observed decrease in particle size is due to a decrease in viscosity of the polymer solution (oil phase). However, further increase in concentration increased the particle size, because plasticizers might have occupied the free-volume space within the matrix, thus hindering the inward shrinkage of the matrix. A decrease in particle size with increasing amount of PCL is observed due to a decrease in polymer solution viscosity (oil phase). High encapsulation efficiency (see Table I) was observed in almost all formulations. This might be due to the poor aqueous solubility of NFD. It may be noted that encapsulation efficiency up to 95% is observed for blank microspheres, while for microspheres with PEG as a coexcipient, lower drug encapsulation efficiency (~70%) is observed. Since PEG is a water-soluble polymer, it might help in solubilizing NFD and its leaching out from the microspheres.

Porous structure of the microspheres was observed by SEM micrographs (Fig. 2), with no free NFD crystals on the surface of the microspheres. As can be seen from the micrographs, because of rapid diffusion of the solvent, larger cavities are formed producing hollow structures [Fig. 2(B)], thereby, making them to float. The CA–PCL-based microspheres exhibit irregular shapes [see Fig. 2(C)]. Figure 2(D) shows the porous structure of CA–PEG microspheres after dissolution experiments, demonstrating that diffusion of the incorporated drug may be highly facile from the channels (pores) created by the diffusion of PEG. An important aspect of the multiparticulate drug-delivery system is that they are to be delivered as a single unit dosage form. This means they should possess the necessary flow characteristics as measured by the angle of repose $\phi$ for the microspheres (see Table I). The values of $\phi$ ranging between 26 and 33° suggest the good flow characteristics of the microspheres,[11] indicating their nonaggregative nature.

### Thermal analysis

To investigate the compatibility of the drug with the polymer and the excipients used, microspheres have been subjected to thermal analysis. From the thermograms of the drug-loaded microspheres containing PEG, DBP, and PCL presented in Figure 3, it is observed that endothermic peak of the blank microspheres of CA at ~93°C has shifted to lower temper-

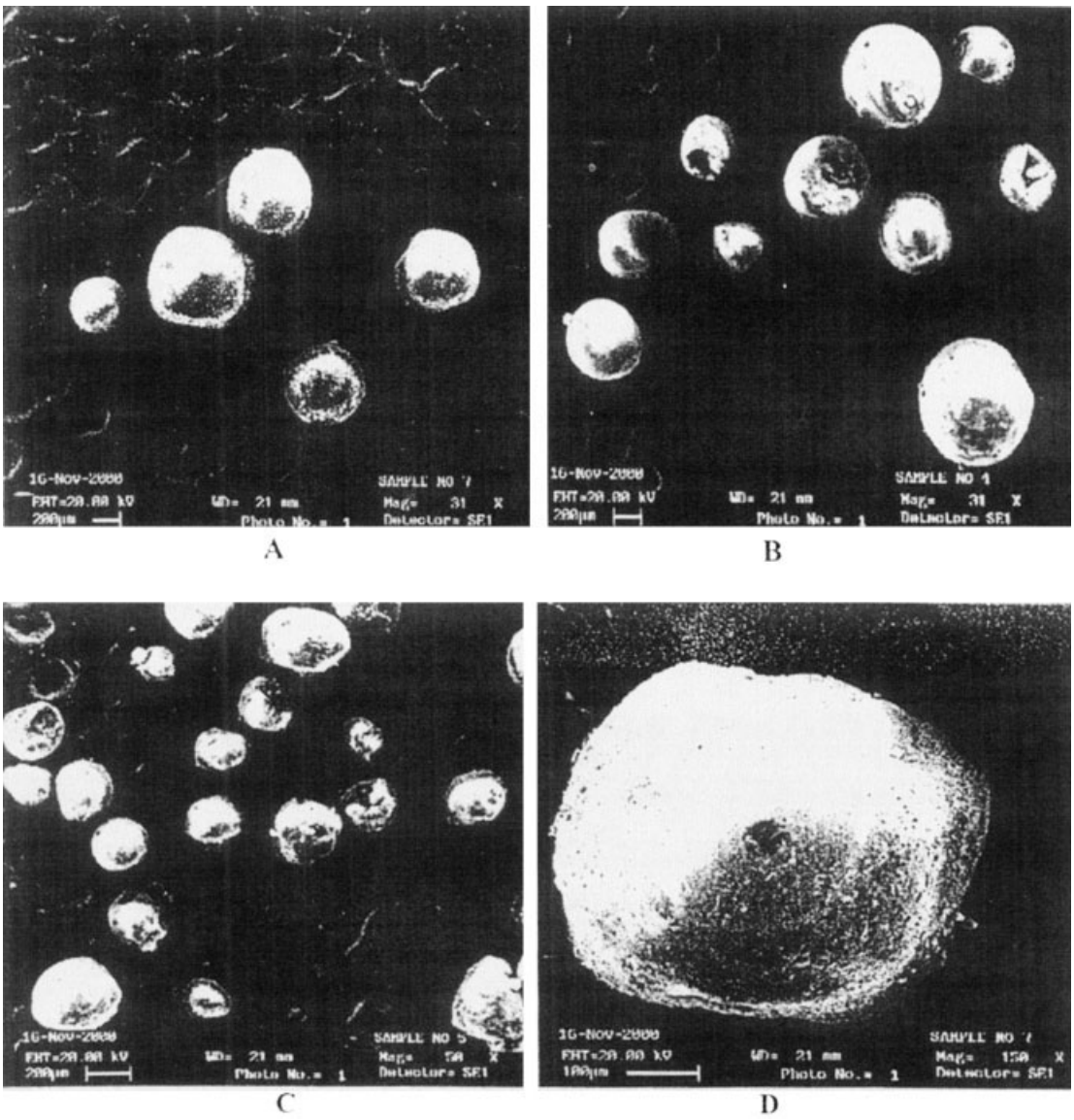


**Figure 2** SEM micrographs of the hollow microspheres: (A) CA–PEG-1, (B) CA–DBP-1, (C) CA–PCL-1, and (D) CA-PEG-1 after dissolution showing the pore formation.

atures with increasing concentration of PEG and DBP. A decrease in enthalpy ($\Delta H$, J/g) with increasing concentration of PEG and DBP is due to the plasticization effect as a result of reduction in attractive forces between the polymer chains.[15,16] This might have shifted the endothermic peak to lower temperatures with lower $\Delta H$ values, thereby, lowering the $T_g$ of the polymer. However, with the blend microspheres, a decrease in endotherm of CA from ~93 to ~80°C is observed for 50% PCL-containing microspheres, since PCL has a lower $T_m$. These results suggest that the excipients exert an effect on molecular mobility of the CA chains. The disappearance of a sharp endothermic peak of NFD at ~173°C (see Fig. 3) in all the formulations indicates that NFD is molecularly distributed inside the hollow microspheres, and no free crystals of NFD are formed on the surface of microspheres. As reported earlier,[14] free drug crystals can be formed if the drug payload is >5% (based on the dry mass of the polymer). In the present study, when 10% NFD is loaded, no free crystals are observed, which was confirmed by both DSC and SEM analyses. This could be due to adopting an interrupted solvent evaporation technique as reported earlier by Benita et al.[17]

### FTIR spectral study

In an effort to investigate the molecular level interactions between drug and the polymer matrix, samples have been analyzed by FTIR. FTIR tracings are presented in Figure 4 for the drug-loaded CA microspheres. The composite peak observed at ~1720–1746

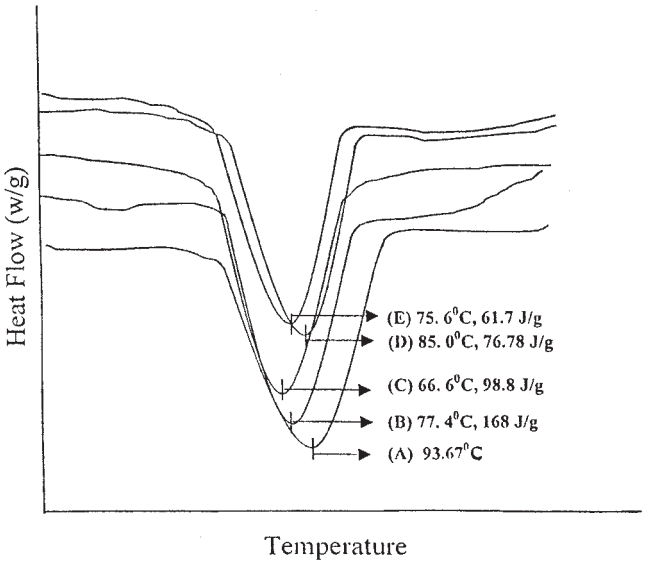


**Figure 3** DSC thermograms of NFD and NFD-loaded hollow microspheres.

$cm^{-1}$ is assigned to carbonyl group of CA, NFD, PCL, and DBP. The absorption peak observed in the region 3481–3499 $cm^{-1}$ is assigned to hydroxyl group of CA, which in the presence of PEG has broadened because of the H-bond formation. In all the formulations, a peak observed at ~3333 $cm^{-1}$ is assigned to —NH stretching. Two strong peaks observed at ~1530 $cm^{-1}$ and ~1433 $cm^{-1}$ for —$NO_2$ group of NFD agree with the literature findings.[18] Thus, FTIR data indicate the absence of chemical interactions between NFD and the polymer matrix.

### Floating properties and in vitro release studies

Floating properties of the hollow microspheres have been studied using 0.1*N* HCl and 0.02 v/v% Tween-80 as a simulated gastric fluid. Coexcipients have an influence on the floating properties. For instance, with CA–PEG microspheres, buoyancy is lower, which increased with increasing concentration of PEG. However, by increasing the concentration of PEG from 10 to 40%, the buoyancy decreases from 51.3 to 11.8%, as PEG might have leached out of the CA matrix, thereby, creating more free channels or pores (Fig. 2(D)). These channels are responsible to increase the water diffusion, which further increases density of the microspheres by decreasing their buoyancy. A better buoyancy of 62–82% is observed for microspheres with water-insoluble plasticizer like DBP after 15 h. This might be due to the fact that DBP is a hydrophobic plasticizer and it prevents wetting as well as water uptake. However, the percentage buoyancy of CA–PCL formulations decreases from 26 to 6 with increasing concentration of PCL (see Table I). As CA–PCL microspheres are smaller in size (268–318 $\mu$m) and have larger surface area with a relatively higher density, and hence, they exhibit lower buoyancy.[11,19] However, floating microspheres are known to retain in the gastric environment for >8 h.[2,20,21] This prompted us to study their in vitro release studies in simulated gastric condition of 0.1*N* HCl for >8 h. Because of their floating nature, microspheres are forcibly immersed into the dissolution media to avoid their adherence to the surface of the dissolution jar, thus avoiding their nonparticipating behavior during dissolution.

Release profiles of the formulations are shown in Figures 5–7; the release of NFD from the blank microspheres is ~21% of the total drug loaded even after 10 h. The type of coexcipients used while preparing the drug-loaded microspheres exerts an influence on the release characteristics of NFD. In case of CA hollow microspheres (see Fig. 5), with increasing amount of PEG in the matrix, the drug release increased considerably compared to the blank. After the addition of 10% PEG, a three-fold increase in the release of NFD is observed after 1 h, but after 10 h, a ~55% of NFD is released. As explained previously, PEG increases the hydrophilicity of the matrix and forms pores/channels, thereby, facilitating the release of water-insoluble NFD. Similarly, increased permeability of sucrose in CA films increased due to the presence of PEG in the matrix.[22] Yeh et al.[23] reported the elimination of lag-phase by effectively engineering the rapid pore formation due to the diffusion of PEG from poly(DL-lactide) microspheres. In the present study, an increase of PEG concentration increased the release rates of NFD. For instance, when the concentration of PEG is increased to 40%, a rapid initial drug release occurred with an increase in the release rate of 54%, and almost 100% NFD was released within 10 h. This is attributed to diffusion of PEG, which might have created more number of water-filled channels, and thereby, facilitating the drug release.

The release profiles of CA–DBP formulations are presented in Figure 6. Initially, a slight decrease in drug release is observed for CA–DBP-1 formulation when compared to the blank. By increasing the concentration of DBP, an increase in the release rate of NFD is observed. For instance, with CA–DBP-3, only 22% NFD is released within the first hour, but 63% of NFD is released after 10 h. According to free volume theory, diffusion occurs by the localized activated jumps from the preexisting cavities to another cavity.[15,16] Results of this study suggest that the rate of drug release is dependent upon the type of the plasticizer used. We found that the effect of PEG on drug release is more than that observed for DBP. In case of PEG, drug release is facilitated due to the creation of microchannels as a result of increased hydration of the microspheres. In an earlier study, it was observed that

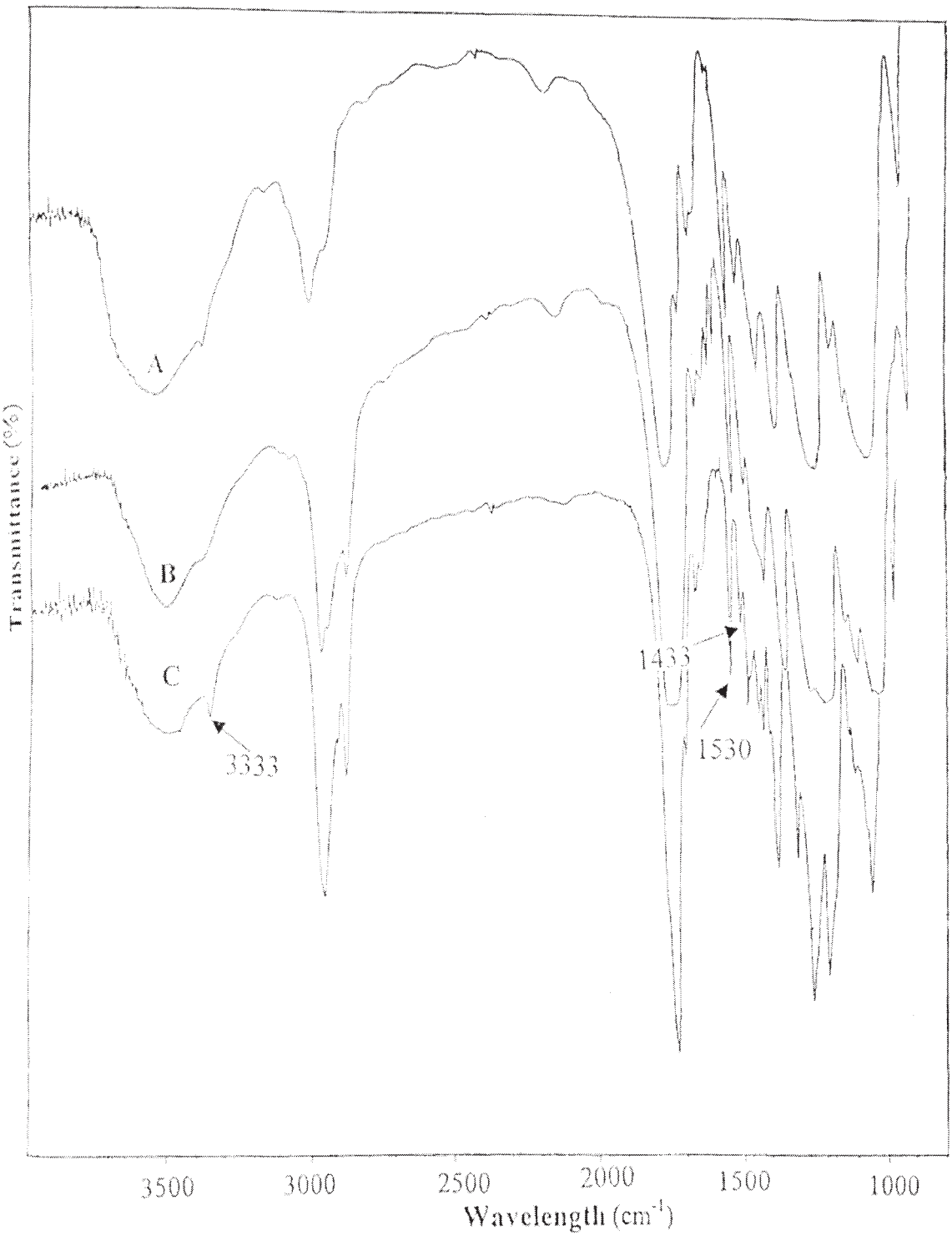


**Figure 4** FTIR spectra of NFD-loaded hollow microspheres: (A) CA–PEG-3, (B) CA–DBP-3, and (C) CA–PCL.

higher diffusion rates are observed for diltiazem and indomethacin drugs when PEG-600 was used as a plasticizer for the CA films when compared to DBP.[9]

The release profiles of NFD from CA–PCL hollow microspheres presented in Figure 7 indicate that by increasing the concentration of PCL in the polymer matrix, drug release also increases. These results can be explained on the basis of the decrease in particle size with an increase in PCL concentration (Table I). Similarly, a decrease in the size of microspheres will increase the surface area and thereby, increases the release of NFD from the microspheres. It is also possible that PCL could influence the NFD release rates, since it has the lower value of $T_g/T_m$ of the micro-

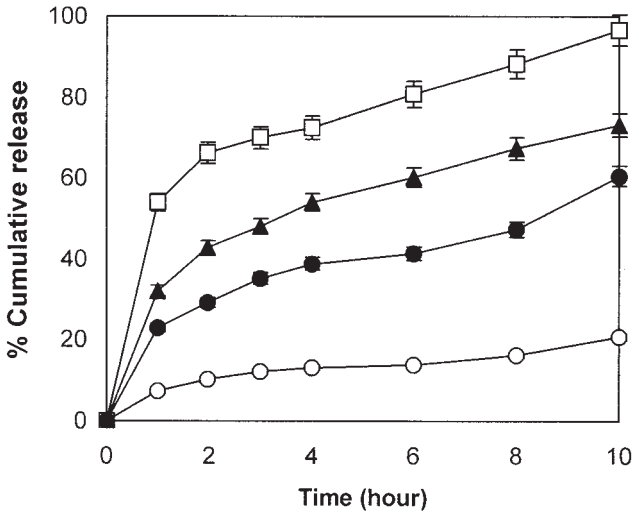


**Figure 5** Release profiles of hollow microspheres: blank (○), CA–PEG-1 (●), CA–PEG-2 (▲) and CA–PEG-3 (□).

spheres; this might have increased the polymer chain mobility to facilitate drug diffusion through the CA matrix. Therefore, it appears that differences in the release rates presented in Figures 5–7 can be explained by the nature of the matrix formed and the coexcipinets used, which could affect the hydration of the matrix during drug release.

### Release kinetics

To understand the release kinetics of NFD through hollow microspheres, release data have been analyzed using the empirical equation[24]

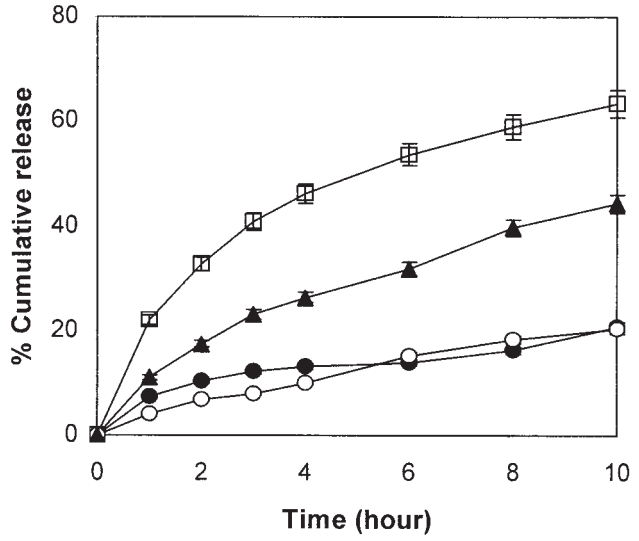


**Figure 6** Release profiles of hollow microspheres: blank (○), CA–DBP-1 (●), CA–DBP-2 (▲), and CA–DBP-3 (□).

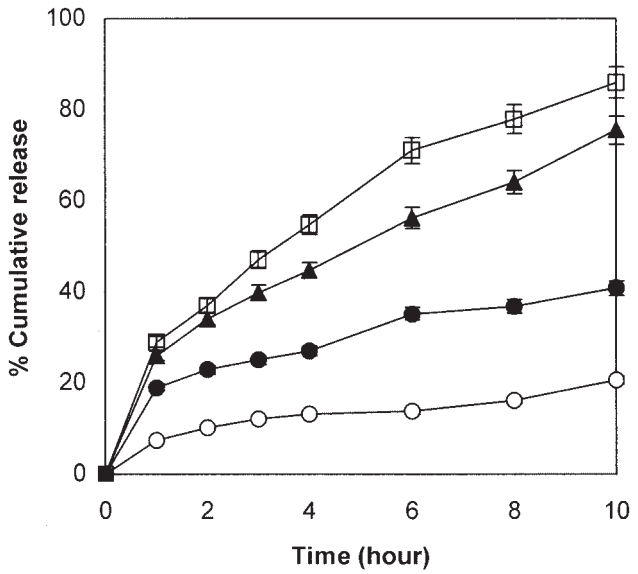


**Figure 7** Release profiles of hollow microspheres: blank (○), CA–PCL-1 (●), CA–PCL-2 (▲), and CA–PCL-3 (□).

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

where $M_t/M_\infty$ represents fractional drug release at time $t$, and $k$ is a constant characteristic of the drug–polymer system; $n$ is the diffusional exponent. If $n = 0.5$, then transport follows Fickian nature. For $n = 1.0$, Case-II transport exists. If the values of $n$ range between 0.5 and 1.0, then the anomalous-type transport[24] is operative. In some cases, the values of $n$ are lower for devices having different geometries. Ritger and Peppas[25] found $n$ values ranging between 0.45 and 0.89 for cylindrical geometry, but for spherical particles, $n$ varied between 0.3 and 0.45, suggesting Case II transport. In our previous study,[26] we have reported still lower values of $n$. The calculated values of $k$ and $n$ along with the correlation coefficients, $r$, are presented in Table II. For CA–PEG-1 and CA–PEG-2

**TABLE II**
**Release Kinetics Parameters of the Hollow Microspheres Calculated from Eq. (4)**

| Formulation code | $n$ | k × $10^2$ $(min)^{-n}$ | Corr. Coeff. $r$ |
|---|---|---|---|
| CA–PCL-1 | 0.33 | 5.35 | 0.979 |
| CA–PCL-2 | 0.46 | 4.06 | 0.996 |
| CA–PCL-3 | 0.55 | 2.58 | 0.988 |
| CA–PEG-1 | 0.23 | 2.12 | 0.985 |
| CA–PEG-2 | 0.24 | 11.07 | 0.962 |
| CA–PEG-3 | 0.46 | 19.92 | 0.998 |
| CA–DBP-1 | 0.70 | 0.23 | 0.993 |
| CA–DBP-2 | 0.62 | 0.86 | 0.994 |
| CA–DBP-3 | 0.49 | 2.90 | 0.996 |
| Blank | 0.31 | 2.12 | 0.990 |

formulations, the values of $n$ are 0.23 and 0.24, respectively, indicating that transport follows Fickian trend. For CA–PEG-3 formulation (i.e., with higher concentration of PEG), drug release follows the non-Fickian trend. The values of $k$ are dependent on the concentration of coexcipients used, i.e., these values increase with increasing concentration of coexcipients.

## CONCLUSIONS

Novel hollow microspheres of cellulose acetate with coexcipients containing nifedipine have been prepared using the solvent diffusion/evaporation method. Coexcipients viz., PEG, DBP, and PCL have shown their effect on floating, physicochemical properties as well as release characteristics of the hollow microspheres. The use of channeling agents or water-soluble plasticizers like PEG has reduced the floating characteristics. The formulation with DBP showed that it is possible to manipulate the release profiles without sacrificing much on their floating properties. Drug-release properties of these microspheres can be easily altered by changing the process parameters. Therefore, hollow microspheres obtained could be the interesting candidates for circumventing the limitation posed by the GRT of oral route of administration in delivering the drug for a longer period of time (>8–12 h). Such systems might be helpful to increase the therapeutic efficacy of the drugs with a therapeutic window at the proximal end of GIT.

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