Preparation, Characterization and Evaluation of a Novel Drug Carrier for the Controlled Release of Curcumin

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ABSTRACT

The upsurge of cancer demands intense, rapid and effective intervention from the scientific society. Even though nanoparticles helped achieving this, maintaining its size without using toxic capping agents is challenging. Phytochemicals having reducing properties is a proper substitute and the efficiency of such nanoparticles could be further improved by grafting with suitable monomers. It could be further protected from rapid biodegradation by coating with suitable materials. This approach was utilized wherein, the green synthesized silver nanoparticles (AgNps) were initially functionalized with –COOH to couple with $-NH_2$ groups of ethylene diamine. It was then coated with polyethylene glycol (PEG) and hydrogen bonded with curcumin. The formed amide bonds could effectively uptake drug molecules and sensed environmental pH. Swelling studies and release profiles confirmed selective drug release. All these results along with those obtained from MTT assay, suggested the potential applicability of the prepared material in pH sensitive drug delivery of curcumin.

Introduction

Drug delivery is a method or process of transporting a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effect [1]. In traditional drug delivery systems like oral ingestion or intravascular injection, the medication is distributed throughout the body through the systemic blood circulation [2]. For most therapeutic agents, only a small portion of the medication reaches the organ to be affected, such as in chemotherapy where roughly 99 % of the drugs administered do not reach the tumor site. Moreover, some medicines may not move easily through the circulatory system or through tissues and cells. Others may lose efficacy as they pass through the digestive system or may cause harmful side effects to healthy organs and tissues.

Currently, many drug delivery systems (DDS) are under investigation for cancer therapy. Cancer in general is a disease which is characterized by the uncontrolled growth and multiplication of cancerous cells. Even though conventional therapies have enhanced patients' survival, they also have numerous drawbacks. For example, in conventional cancer chemotherapy, the therapeutic agents distribute non-specifically in different tissues of the human

body, thus affecting both cancerous as well as normal cells [3]. This non-specific distribution of drugs to normal cells, tissues and organs cause excessive toxicities thereby causing numerous adverse drug reactions including alopecia, weakness, organ dysfunction etc. [4]. So a new method called "targeted drug delivery" came to the scene where the medication is selectively delivered to its site of action or absorption and not to the non-target organs or tissues.

Now a days nanotechnology works on the design and development of many novel formulations for the prevention, treatment and diagnosis of many critical diseases like cancer, T.B, cardiovascular diseases etc. Nanoparticles with specific functional properties can be used as drug carriers in DDS. Non-toxicity, biocompatibility, water-dispersibility and narrow size distribution are some of the primary requirements for nanoparticles to be used as drug carriers [5]. A critical step in developing such carriers is to engineer the surface of nanoparticles with suitable bioactive molecules. Recently, organic and inorganic functionalities were being introduced on the surface of nanoparticles namely carboxylate, phosphate, phosphonates, amines, organosilane, silica and gold which proved to possess better efficacy without affecting the properties of nanoparticles [6]. The presence of these organic/inorganic layers on surface not only stabilizes the nanoparticles, but also provides desired properties required for encapsulation of drugs. Further, the selective binding of specific functional groups on nanoparticles surface provides stimuli responsive shell that is susceptible to external environments such as pH, temperature, ionic strength, ultrasound intensity, enzyme, light, electric pulses etc. The stimuli responsive shell ensures that the loaded drug molecules will not freely extravagate during blood circulation, i. e., the drug should not be released before reaching target tissues, but only to be released at the target sites. Owing to physiological differences between cancerous and normal cells, pH-sensitive nano carriers represent smart vehicles for transport and delivery of anticancer drugs [6].

Silver nanoparticles (AgNps) are one of the most vital and fascinating nanomaterials among several metallic nanoparticles that are involved in biomedical applications. AgNps have been focused on potential applications in cancer diagnosis and therapy. AgNps can act as antibacterial, antifungal, antiviral, anti-inflammatory, anti-angiogenic and anti-cancer agents [7]. They are also used in various fields, including medical, food, health care, consumer and industrial purposes, due to their unique physical and chemical properties. AgNps can be prepared using physical, chemical and biological methods. The advantages of physical methods are speed, radiation used as reducing agents, and no hazardous chemicals, but the downsides are low yield and high energy consumption, solvent contamination and lack of uniform distribution. Chemical methods use three main components, such as metal precursors, reducing agents, and stabilizing or capping agents. The major advantage of chemical methods is high yield, contrary to physical methods, which have low yield. But, the disadvantage is that the materials used for AgNps synthesis, such as citrate, borohydride, thio-glycerol and 2-mercaptoethanol are toxic and hazardous. Apart from these, the manufactured particles are not of expected purity, as their surfaces are found to be sedimented. It is also very difficult to prepare AgNps with a well-defined size, requiring a further step for the prevention of particle aggregation [8]. In biological synthesis the materials used are eco-friendly and pollution-free and also eliminate the need of prevention of particle aggregation. However, these methods are expensive. Considering these facts, chemical synthesis is best suited if the use of toxic reagents could be avoided. Further, carboxyl functionalized silver nanoparticles exhibit much better dispersity and stability in aqueous solution [9–11]. Furthermore, drug-loaded nanoparticles exhibit noticeable pH-sensitive behaviour with accelerated release of drug in acidic environment. Compared with native nanoparticles, carboxyl functionalized nanoparticles show enhanced intracellular uptake efficacy and stronger effect on killing tumor cells [12–14]. They can also be located in cytoplasm and can accumulate in tumor tissues for longer periods of time. Further, these surface carboxyl groups can be functionalized through well-known peptide coupling reactions [15, 16].

In order to deliver adequate concentrations of systemically administered therapeutics to target tissues, these materials must circulate in the blood stream for as long as possible. However, recognized as foreign objects, nanoparticles are readily cleared from systemic circulation by the cells of the mononuclear phagocyte system, necessitating approaches for increasing circulation time. One such approach is to coat the surface of nanoparticles with an inert polymer that resists interactions with components of the blood stream, imparting "stealth" properties. Polyethylene glycol (PEG) is the most widely used "stealth" polymer in the drug delivery field. PEG is a polyether compound with many applications from industrial manufacturing to medicine. PEGylation could also shield the surface from aggregation, opsonisation and phagocytosis, thereby prolonging circulation time [17].

Due to its hydrophilic nature, PEG chains grafted on nanoparticles generate a hydrated cloud with a large excluded volume that sterically precludes nanoparticles from interacting with neighbouring nanoparticles and blood components [17]. In addition, the large conformational freedom provided by the flexibility of PEG renders interpenetration of foreign matters into the PEG corona which make it thermodynamically unfavorable.

Curcumin (CUR) has received immense attention over the past decades because of its diverse biological activities, including anticancer, antioxidant, anti-amyloid, anti-inflammatory, antidiabetic, antibiotic and antiviral activities [18]. Hence, CUR is recognized as a promising drug candidate in a large number of diseases such as cancer, neurodegenerative diseases, infectious diseases and diabetes. However, the application of CUR in therapeutic treatment has been hindered due to three obstacles. The first obstacle is its extremely low aqueous solubility. Its maximum water solubility is about 30 nM, whereas the required concentration to exhibit various bioactivities lies in micro molar regime. Therefore, it is necessary to dissolve curcumin in appropriate organic solvents. The second obstacle is its chemical instability in aqueous condition. CUR is quickly hydrolyzed under physiological pH 7.4 in phosphate buffer with a half-life ($t_{1/2}$) of only 20 min. The third obstacle is low cellular uptake. However, CUR encapsulated AgNps has been reported to show potential activity against cancer cells [19].

In the present study a hydrophilic matrix was designed and developed to encapsulate a hydrophobic drug - CUR. This was achieved by reacting the carboxyl functionalized AgNps with the aliphatic chains of ethylene diamine. To these aliphatic chains, CUR

was loaded to ensure hydrophobic – hydrophobic interactions between the drug and the polymer. To the amide functionality, PEG was coated, to achieve sufficient hydrophilicity in aqueous physiological environment. Even though many reports in this direction has already been published, the main focus of the present investigation was to overcome the side-effects of cancer chemotherapy by pH guided drug release leading to more accumulation of the drug molecules at malignant sites rather than at normal cells.

Materials and Methods

Materials

$AgNO_3$ (CAS No.: 7761–88–8), N-Hydroxysuccinimide (NHS, CAS No.: 6066–82–6), Ethylene diamine (CAS No.: 107–15–3), PEG (CAS No.: 25322–68–3) and CUR (CAS No.: 458–37–7) were obtained from Merck Chemicals, India. Lactic acid (CAS No.: 50–21–5) was purchased from Spectrum Reagents and Chemicals Pvt. Ltd, India. Acetone and diethyl ether were obtained from Nice Chemicals Pvt. Ltd, Kochi, India and Merck Life science Pvt. Ltd, Mumbai, India respectively. 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC, CAS No. 25952–53–8) was procured from Tokyo Chemical Industry (TCI), Tokyo. All other chemicals used in this study were analytical grade and used without any further purification. Neem leaf was collected from Nemmara N. S. S. College during the summer season of March. Fresh and tender leaves were carefully hand plucked, washed with distilled water to remove dust and other impurities, cut to fine pieces and sun dried in shade for a minimum of three days and used. Doubly distilled water with conductivity less than 1 μcm^{-1} was used throughout the experiments.

Characterization of the Drug Carrier

All the reaction steps were monitored using ATR spectra recorded using Agilent CARY 630 ATR Spectrometer in the frequency range 4000–650 cm^{-1} by direct sampling technique. XRD patterns of the samples were examined using Siemens D5005 X-ray source. The size and charge of samples were studied using DLS, performed on Horiba SZ-100 equipped with a 532 nm Diode Pumped Solid State (DPSS) laser, operated at a temperature of 25°C. Prior to DLS analysis, all samples were dispersed using an ultra sonicator for definite periods of time to avoid aggregation (PCi Electronics, Mumbai, 230 V, 50 Hz). Scanning electron microscopy (SEM) analysis were carried out using a Carl Zeiss EVO-18 scanning electron microscope operated in vacuum at 15–20 kV having a working distance of 12 mm. All the samples were sputter coated with thin gold layer to make the surface conductive towards the electron beam. pH measurements were made on a μ processor Systronic pH meter (model MKVI, Ahmedabad, India). Absorbance measurement of drug solutions were performed on Thermo Scientific UV-Visible spectrophotometer (model- Evolution 220).

Preparation of the Drug Delivery System

Green Synthesis of AgNps

Since being designed to use at physiological conditions, use of chemical capping agents were replaced with herbal extracts of neem leaves. These extracts have abundance in reducing agents like lecithins and anthocyanins and can also act as efficient capping agents as reported by [20]. Briefly, 3.6 mg $AgNO_3$ (w/v) was accurately weighed and added to 20 mL (v/v) water. The solution was boiled with constant stirring using a magnetic stirrer. 20 g (w/w) of finely cut neem leaves were boiled in 100 mL (v/v) water for 30 minutes and filtered to obtain neem leaf extract. 3 mL of this extract was mixed with $AgNO_3$ solution. A colour change from pale yellow to yellowish brown was observed indicating the formation of AgNps.

2.3.2. Synthesis of Carboxyl Functionalized AgNps

5 mL (v/v) AgNp solution and 2 mL (v/v) 1 mM lactic acid were mixed and stirred vigorously for 8 hours in a magnetic stirrer at room temperature. The stirring rate was increased progressively with the development of viscosity of the solution. The obtained white pasty mass was then separated by centrifugation at 2000 rpm for about 15 minutes at room temperature to obtain –COOH functionalized AgNps.

Synthesis of Carboxyl Functionalized AgNps

Amide bonds enhance drug encapsulation. To form amide bonds, AgNps should be –COOH functionalized. The most common procedure is with lactic acid. The importance of lactic acid is that it is biodegradable as well as chemically stable. Briefly, 5 mL (v/v) AgNp solution and 2 mL (v/v) 1 mM lactic acid were mixed and stirred vigorously for 8 hours in a magnetic stirrer at room temperature. The stirring rate was increased progressively with the development of viscosity of the solution. The obtained white pasty mass was then separated by centrifugation at 2000 rpm for about 15 minutes at room temperature to obtain –COOH functionalized AgNps.

Drug Loading

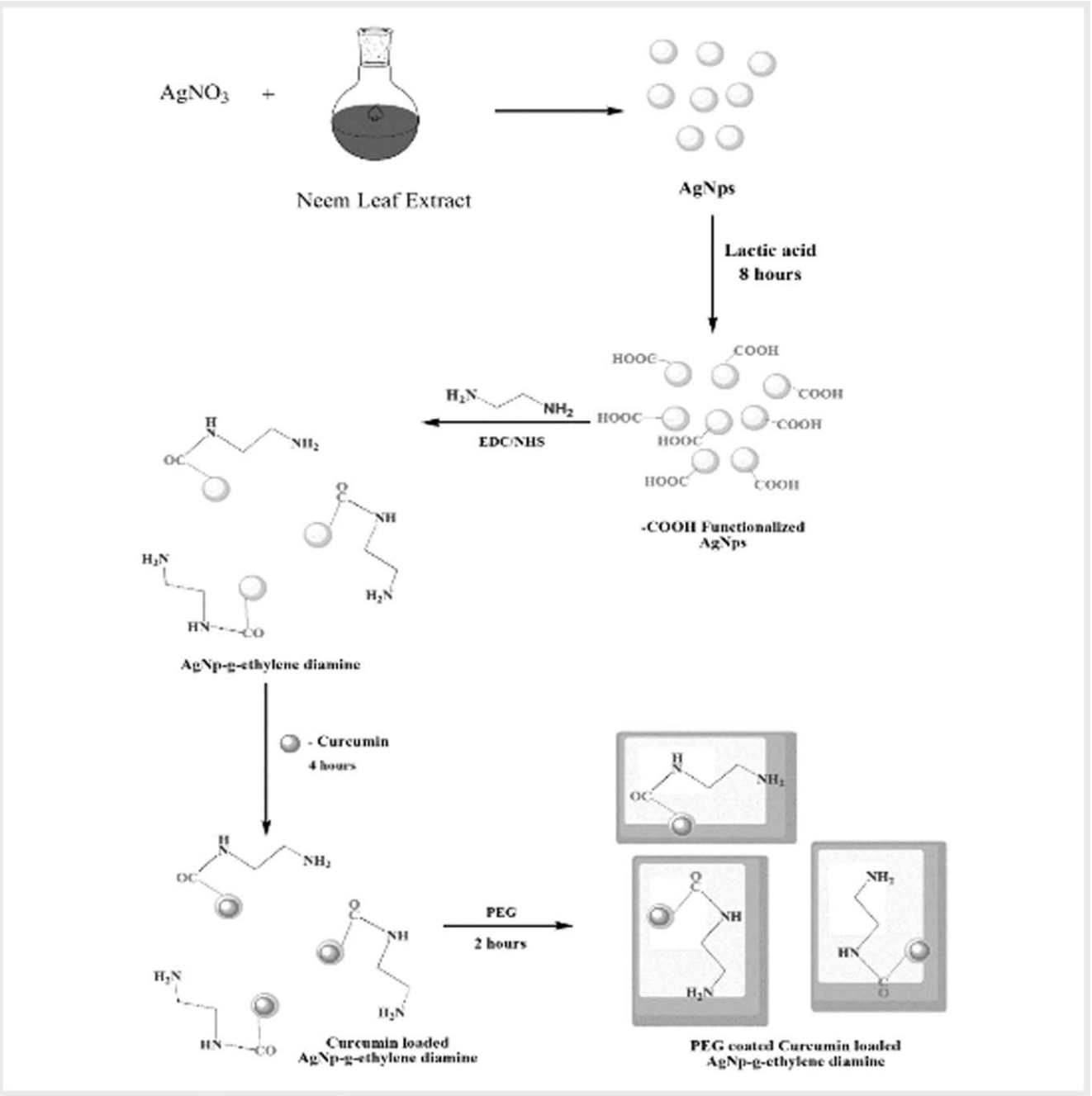
0.5 g (w/w) amide functionalized AgNps was weighed, dispersed in 2 mL water and mixed with 0.25 g (w/w) CUR. To this solution, 5 ml (v/v) water was added and shaken well for 4 hours. The amount of drug loading, encapsulation efficiency and theoretical loading % were calculated using the following equations:

PEGylation of Drug Loaded System

In order to provide stability in aqueous medium and to act as a barrier for drug release, the synthesized drug carrier was coated with PEG. Concisely, 0.75 g (w/w) PEG was dissolved in 7.5 mL (v/v) water. It was added to 1.0 g (w/w) of the drug loaded sample and shaken well for 2 hours at room temperature. It was then dried at around 70°C for 1 hour and used for the studies. A schematic diagram for the preparation of the drug carrier is as shown in ▶ **Fig. 1** below.

In Vitro Drug Release

In vitro release studies were carried out in phosphate buffered saline media of pH 7.4 and simulated gastric fluid at pH 1.2 using dialysis bag technique. Briefly, 0.825 g (w/w) of the PEGylated drug loaded sample in 5 mL buffer solution was taken in dialysis bag and was dipped in receptor compartment containing 300 mL dissolution medium, which was shaken at 37 ± 0.5°C in Julabo shaking water bath (SW23). The receptor compartment was closed to prevent evaporation. The shaking frequency was kept constant at 100 rpm. 5 mL of the sample was withdrawn at regular intervals and was replaced with fresh dissolution medium. Samples were ana-



▶ **Fig. 1** Preparation of the Novel Curcumin Loaded Drug Carrier.

lyzed for the drug content, curcumin by UV-Vis spectrophotometer. Experiments were performed in duplicate and the average values were used in data analysis.

2.3.7. pH-Responsive Equilibrium Swelling Study

Swelling studies of the PEGylated drug loaded sample was carried out in respective buffer solutions. Experiments were carried out by immersing the samples in pre-weighed dialysis bags in acidic and basic buffer solutions. The weights of swollen nano composites were measured at different time after removing the surface water with filter paper. Degree of swelling was measured using equation (4) as:

$$\text{Degree of Swelling}\,\% = \frac{Ws - Wi}{Wd}$$

Where, 'Ws' is the weight of swollen polymer at a given time during swelling. 'W_i' is the initial weight of the sample and 'W_d' represents the dry weight.

2.3.8. Assessment of Cytotoxicity

MTT assay was used to ascertain the selective toxicity of the prepared material towards cancer cell lines. The assay was performed on colorectal cancer cell lines - HCT-116 and normal skin cell line - HaCaT. The seeds of the cell were suspended in a 96-wellplate at a required cell density of 25,000 cells per well and the cells were allowed to adhere the culture plate for about 24 hrs. Appropriate concentration of the test reagent was added to the plate and was incubated at 37°C in 5 % CO_2 atmosphere. 10 % MTT reagent to the total volume was added. This volume was kept same to that of the standard sample and was used to determine optimum cell density after 3 hrs of incubation. For adherent cells, the culture medium was aspirated without disturbing the mono layer. Solubilisation solution - DMSO in equal amount was added to the culture number. Gentle stirring to enhance the dissolution was done occasionally as well as pipetting up and down to completely dissolve the MTT formazan crystals especially in dense culture. Absorbance was measured at 570 nm. All the experiments were performed twice, and the relative cell viability (%) was expressed as a percentage relative to the untreated control cells as shown in equation (5) as:

$$\text{Cell viability}\,(\%) = OD_{test}/OD_{control}$$

Statistical Analysis

Data were expressed as means of three separate experiments, and were compared by analysis of variance (ANOVA). A p-value < 0.05 was considered statistically significant in all cases.

Results and Discussion

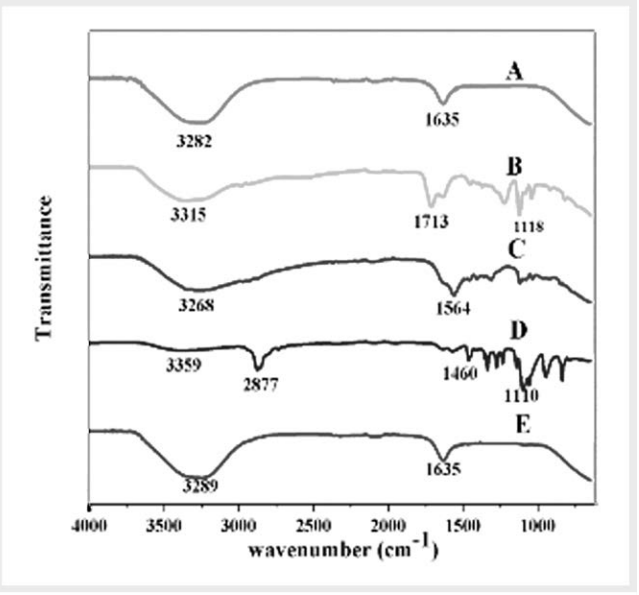
This section can be divided into two parts. The first section deals with the characterization of the prepared material using different techniques like FTIR, XRD, DLS, Zeta potential and SEM. The second section deals with evaluating the efficiency of the material as a drug delivery device wherein, the *in vitro* drug release, equilibrium swelling studies, release kinetics and MTT assay were performed.

Characterization of the Prepared Drug Delivery System

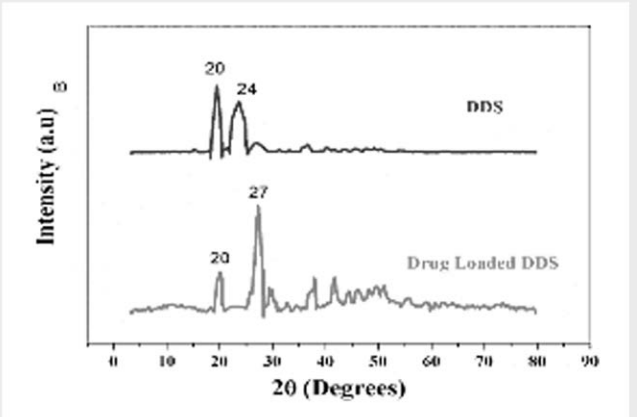
Attenuated Total Reflectance (ATR)

Synthetic strategy involved formation of amide bonds between carboxyl functionalized AgNps and ethylene diamine by carbodiimide chemistry with the subsequent coating by PEG. The superior yield and purity of this step might be due to carbodiimide reagent. By using the EDC catalyst, the carboxyl group of AgNps could form an active ester intermediate which further reacted with the primary amino groups of ethylene diamine, forming an amide peptide bond. This strong bond stabilizes the polymeric material. All the reaction procedures were carefully monitored using ATR and the obtained spectrum is as shown in ▶ **Fig. 2**.

In the ATR spectra of AgNps (▶ **fig. 2a**), the characteristic peak of silver nanoparticles were observed at 1635 cm^{-1}. After carboxyl functionalization, broad peaks at 3315 cm^{-1} owing to hydroxyl groups were observed (▶ **fig. 2b)**. Importantly, peak at 1713 cm^{-1} due to carboxyl functionality was also observed. On coupling carboxyl functionalized AgNps with ethylene diamine, a new peak owing to the formation of 1° amide bond was observed at 1564 cm^{-1} (▶ **fig. 2c**). Upon coating with hydrophilic PEG, new peaks appeared at 3359 and 2877 owing to the hydroxyl functionality and aliphatic carbon chain vibrations (▶ **fig. 2d)**. These data confirmed successful PEG coating. Further, the hydrogen bonding interaction between the polymer and PEG was confirmed by the broad peaks above 3000 cm^{-1}. After loading with CUR, small shoulders in the range 1200–1500 cm^{-1} appeared due to the functionalities present in the phenolic drug – curcumin (▶ **fig. 2e**). In addition, all the characteristic peaks of the monomers and PEG was well maintained in the drug loaded sample revealing that all the designed reactions were suitable enough to achieve the desired product.



▶ **Fig. 2** ATR spectra of **a**) AgNps, **b**) –COOH functionalised AgNps, **c**) AgNp-g-ethylene diamine, **d**) PEG@AgNp-g-ethylene diamine and **e**) Curcumin loaded PEG@AgNp-g-ethylene diamine.



▶ **Fig. 3** XRD spectra of DDS and Drug loaded DDS.

X-ray Diffraction (XRD)

The XRD pattern of DDS and drug loaded DDS are as shown in ▶ **Fig. 3**. XRD pattern mainly depicts the crystallinity and inter planar distance of the samples. XRD pattern of DDS shows a characteristic peak at 20 and 24° owing to the presence of AgNps. Thus, the synthesis of nano silver was confirmed. When loaded with CUR, the sample exhibited broad peaks confirming the increase in surface area of the sample after drug loading. This would result in uniform drug release as well as repeatable and reproducible results in drug delivery. In addition, evidence for successful drug loading was evident from the characteristic peaks of CUR at 27 and 51°.

Dynamic Light Scattering (DLS) and Zeta Potential

Hydrodynamic diameter and zeta potential are important criterions for assessing the stability of the material in physiological environment and is as shown in ▶ **Table 1**. As evident from the table, the size of AgNps fall well within the nano regime. Zeta potential values, which are a function of aqueous stability was within the unstable range of – 30 mV to + 30 mV. However, upon introduction of carboxyl groups, the size increased to 51 nm, which might be the consequence of aggregation. The negative potential might be due to the deprotonation of acidic groups. The grafted polymer sample showed a steep increase in size to 119 nm. The zeta value improved to 20.4 mV, but was still unstable. Thus, to stabilize the polymer, it was coated with hydrophilic PEG coating and the size increased to 143 nm. Importantly, the zeta values improved to 31.1 mV, showing that the final material is stable in physiological environment. On loading the drug molecules, the successful entrapment was observed from the increase in size to 179 nm, ensuring efficient interaction between the drug and polymer. Lower particle size favors increased drug uptake as reported previously from our group [20]. The zeta values improved to 34.1 mV which further confirmed that the fabricated material is an efficient candidate in drug delivery at physiological environments.

▶ **Table 1** DLS and zeta potential values of AgNps, AgNp-COOH, AgNp-g-ethylene diamine, PEG@AgNp-g-ethylene diamine and CUR loaded PEG@AgNp-g-ethylene diamine

Sl. No.	Sample	Hydrodynamic diameter (nm)	Zeta Potential (mV)
1.	AgNp	34	– 1.9
2.	AgNp-COOH	51	– 3.4
3.	AgNp-g-ethylene diamine	119	20.4
4.	PEG@AgNp-g-ethylene diamine	143	31.1
5.	CUR loaded PEG@AgNp-g-ethylene diamine	179	34.1

Scanning Electron Microscopy (SEM)

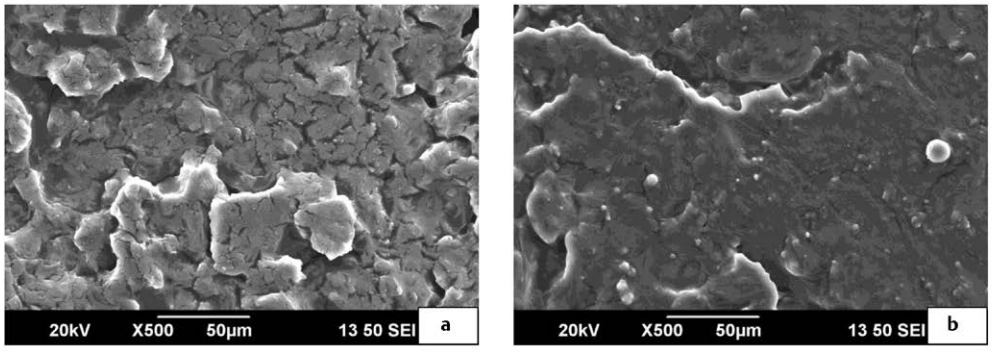
SEM images of PEG@AgNp-g-ethylene diamine and CUR loaded PEG@AgNp-g-ethylene diamine are as shown in ▶ **fig. 4**. The surface morphology was observed to change upon drug loading. For the polymeric sample, the surface morphology appeared to be rough. Homogenous nature of the surface was observed. Even then, several pores could be seen which is indicative of the adsorption power of the polymer. These surface pores could ideally adsorb sufficient CUR. This was evident from the SEM image of the CUR loaded sample where the pores were not much visible. In addition, morphology changed to a smooth surface which could help in uniform and reproducible drug release results. The closure of surface pores could also help in preventing premature leakage of CUR.

Efficiency of the Drug Delivery System

The drug loading and encapsulation efficiency of the prepared polymeric material were evaluated in varying pH values and were calculated using equation 1, 2 and 3. For the present drug delivery system, the encapsulation and loading efficiencies were found to be 51.3 % and 95.8 % respectively. Theoretical loading was found to be 18.6 %. The extensive possibility of hydrogen bonding between the polymer and curcumin could be the reason for these high values.

Equilibrium Swelling Studies

The equilibrium swelling studies of the polymeric material at pH 1.2 and 7.4 were obtained as shown in ▶ **fig. 5**. It can be seen that swelling increases with time and reaches almost saturation around 3 h for pH 1.2 and after 7 h for pH 7.4. In addition, the swelling percentages of all the samples at pH 7.4 are higher compared with



▶ **Fig. 4** SEM images of **a**) PEG@AgNp-g-ethylene diamine and **b**) CUR loaded PEG@AgNp-g-ethylene diamine.

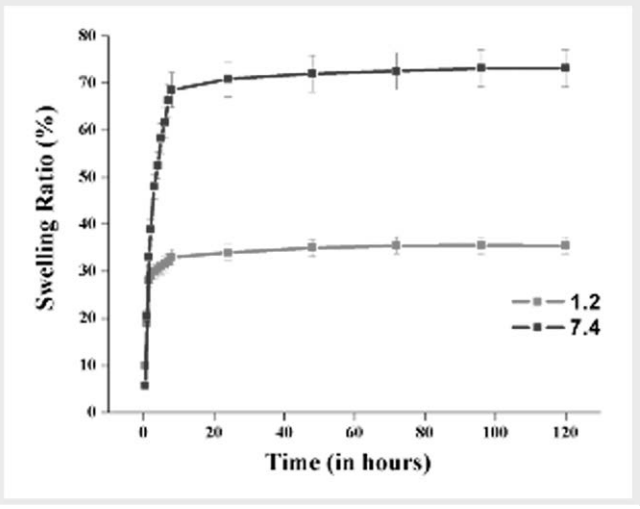
those of same samples at pH 1.2, indicating the selective swelling of the material. The selective swelling of the material could be attributed to the presence of amide bond as previously reported [21]. This was further confirmed by the *in vitro* drug release profiles.

In vitro Drug Release Profile

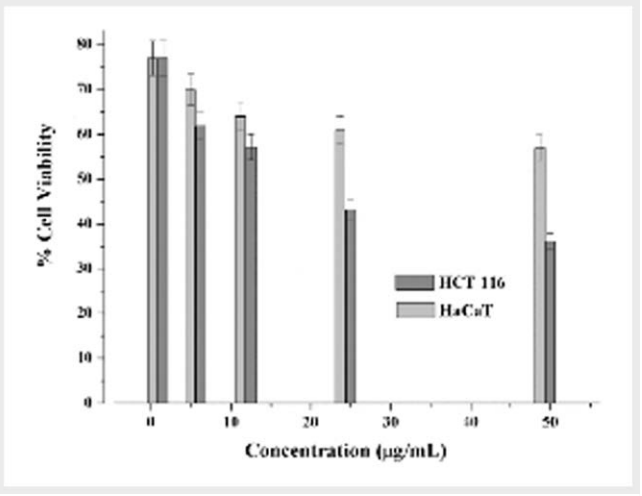
Drug release behaviour of the formulations were evaluated by performing the *in vitro* release experiments in simulated gastric and intestinal pH conditions and the obtained results are as shown in ▶ **fig. 6**. The release rate was found to be high in case of formulations containing higher amount of drug and lower for formulations having lower amount of drug. Thus, release rate was found to be dependent on the drug concentration. The drug release profile showed an initial (1–2 h) burst release of CUR, by breaking the hydrophilic and hydrogen bonding interaction. Thus, very less amount of drug could be expected to be leached from the polymer at pH 1.2. At pH 7.4, controlled release was observed. This pH sensitivity could be attributed to the pH sensitive behaviour of amide bonds as reported elsewhere [21]. Thus, the present material could be considered as a potential candidate for the controlled release of anti-cancer agents at physiological pH. However, the very less percentage release of curcumin at acidic pH could lead to minimal drug delivery at tumor environment as well.

MTT Assay

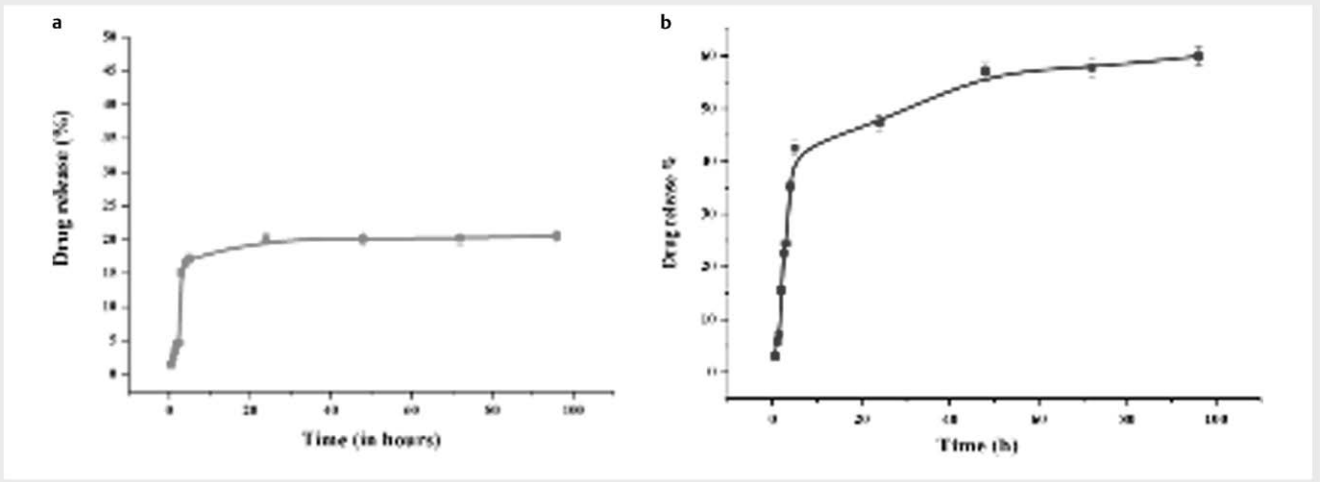
The selective delivery of CUR was ascertained by MTT assay on human colon cancer cell line – HCT 116 and human keratinocyte cell line – HaCaT. The data obtained is as shown in ▶ **fig. 7**. The drug loaded samples were treated with the cell lines at fixed concentrations of 1.5, 6.25, 12.5, 25.0 and 50.0 µg/mL. At lower concentrations, the discriminatory power of the DDS between healthy and malignant cells are low. However, when the concentration of the



▶ **Fig. 5** Swelling studies of the Drug Delivery System at pH 1.2 and 7.4.



▶ **Fig. 7** MTT assay of CUR loaded drug delivery system on HCT 116 and HaCaT cell lines.



▶ **Fig. 6** In vitro release of CUR from the drug carrier at A) pH 1.2 and B) pH 7.4.

DDS increases, a clear distinction in the number of survived cells are visible. The viability % of healthy cells become greater than that of cancerous HCT – 116 cell lines. At the highest concentration of 50.0 µg/mL, only 31 % HCT – 116 cells survived whereas, it is 57 % for HaCaT cells. This proves that the prepared material is a potential candidate for the controlled release of CUR with more bioaccumulation in malignant sites rather than healthy sites.

4. Conclusions

In the present work, a novel drug carrier of AgNp-g-ethylene diamine coated with PEG was designed, synthesized and characterized as a potential candidate for the controlled delivery of curcumin. All the synthetic strategies were scrutinized using instrumental techniques like ATR, XRD, DLS, zeta potential and SEM studies. The swelling capabilities of the prepared samples in varying pH were evaluated. The pH sensitive groups incorporated into the material exhibited sufficient pH sensitivity to be used in tumor environment as observed from *in vitro* drug release profiles. As the preliminary data are promising, *in vitro* MTT assay on normal and cancerous cell lines, followed by *in vivo* analysis are to be performed. From the results obtained, the present material seem to be a promising candidate for the economical and patient compliant chemotherapy with minimal toxicity towards healthy cells.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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