RESEARCH ARTICLE

# Poly Ethylene Glycol-Stearate polymer in the design of nano-drug delivery system for oral administration by curcumin

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**ABSTRACT**

Poly Ethylene Glycol- Stearate (PEG-SA) is used to prepare coated solid lipid nanoparticles (NPs) in the present work with loading curcumin extracted by Turmeric powder (cur-polymer coated-SLNs) by the micro emulsification method. Evaluation of the kinetic release of prepared nanoparticle was resulted. Particle size, zeta potential and polydispersity index were evaluated by Photon Correlation Spectroscopy (PCS). The particle size and zeta potential of cur PEG coated-SLNs were measured as 153 nm. Differential scanning calorimetric indicated that the majority of curcumin loaded in PEG-NP were in amorphous state which is desirable for drug delivery. Drug entrapment efficiency (EE) was 99%. The modification procedure led to a reduction in the zeta potential values, varying from -40.0 mV for the uncoated particles to -23 mV for that of (PEG-SA)-coated NP. FT-IR spectra and HPLC analysis of plain SLNs and pure curcumin exhibited no peak shifting and no loss of characteristic functional group peaks. Shape and surface morphology of particles were determined by transition electron microscopy and scanning electron microscopy that revealed the spherical shape of nanoparticles. The *In vitro* curcumin release of (PEG-SA)-coated SLNs and SLNs showed slight decrease performed for PEG-SA-SLNs one because of coating impact of covering layer.

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## INTRODUCTION

Recently, expanding consideration was routed to solid lipid nanoparticles (SLNs), on account of their biodegradability and capacity to ensnare a diversity of natural dynamic mixes (Biologically active compounds) [1], in the zone of changed drug delivery technology to defeat disadvantages in traditional measurements [2-4]. In addition, SLNs indicate a selective alternative to the conventional colloidal drug delivery systems [3], for example, liposomes, emulsions, and polymeric small scale and nanoparticles (NPs), since the issues identified with modern creation scale-up, sanitization, and mid-term storage are decreased [4-6]. SLNs are made out of a solid lipid matrix regularly secured with a surfactant or phospholipid layer; for sure, their fundamental benefit of drug delivery (below 1000 nm) and to the nearness of physiological or biocompatible lipids or lipid particles, strong at room conditions, with a background marked by immune utilization in treatment. Lipophilic, just as hydrophilic medications (according to hydrophobic particle matching or lipophilic ace medication planning), can be stacked in SLNs with high ensnarement effectiveness. In the course of the most recent 20 years, a few strategies for SLN creation have been completely portrayed in writing: high-pressure homogenization [4-6], hot micro emulsions [5], dissolvable based techniques, for example, dissolvable infusion , dissolvable dispersion or dissipation from oil in water (O/W)

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emulsion, and unsaturated fat coacervation [6-8]. This amphiphilic block polymer has been extensively evaluated for toxicity in animals and is widely used in pharmaceutical formulations and cosmetics, generally regarded as an essentially nontoxic and nonirritant material [9]. A few examinations have been additionally progressively centered on improving their strength in body liquids after organization by coating particles by hydrophilic polymers like poly (ethylene) glycol (PEG) subsidiaries [10,11,12].

Curcumin, a phenolic compound from the plant Curcuma Longa as a customary zest have numerous pharmacological exercises including: anti-diabetic, anti-inflammatory, anti-cancer, anti-oxidant, antibacterial, anti-HIV and anti-aging activity and hepato defensive action just as cardiovascular advantages [13]. Curcumin is an ineffectively water-dissolvable medication with low oral bioavailability and touchy to photo degradation. Utilization of lipids for bioavailability improvement of poor dissolvable medications is promising. Since the vast majority of the segments associated with plan of solid lipid nanoparticles are of common source, they are perfect with segments of organic layer, and for the most part less toxicological hazard is encountered. The principle favorable circumstances of this examination is to adjust the outside of strong lipid NPs for expanding intestinal ingestion and diminishing nanoparticles take-up by invulnerable framework because of incomplete balance of solid negative or positive charge on nano carrier surface [14-16]. In addition, surface alteration of strong lipid NPs by covering a hydrophilic polymer for example PEG-SA resulted in improvement of surface hydrophilicity of NPs which brings about augmentation of nanoparticles transmucosal transport for tranquilize conveyance by nasal, oral and visual way [11,13,17]. Controlled discharge effectiveness and intestinal the wrapped drug obliteration in the stomach and digestive system and likely ingestion of drug through the intestinal mucosa are two diverse assimilation models of medication [18-20]. PEG-SA polymer possessing bioadhesive property can help in devising a delivery system capable of delivering a bioactive agent for a prolonged period of time at a specific delivery site. The intestinal ingestion of medication was accepted as a notable and particular way. Up to now, there is no report on using PEG-SA coated solid lipid nanoparticles carrier for curcumin oral administration therefore future clarification of the parameters governing particle uptake will surely lead to the design of new and more efficient colloidal carriers.

The main approach of the present study is to develop a new nanoparticulate carrier for a hydrophobic drug to be used in oral administration. Colloidal drug carriers prepared from solid triglycerides have been presented as a promising alternative to polymer nanoparticles. The present work is aimed at developing surface modified lipid nanoparticles intended to encapsulate curcumin within their structure and to study their physicochemical properties and *in vitro* stability in gastrointestinal fluids. The final goal is to explore their potential as oral delivery vehicles for macromolecules. The new carrier is composed of a lipid core aimed to protect and control the release of the curcumin that is supposed to facilitate the interaction of the carrier with the intestinal mucosa and the further transport of the hydrophobic drug.

The present research is planned for creating surface altered lipid NPs proposed to encapsulate curcumin inside their framework and to examine their physicochemical features and *in vitro* dependability in gastrointestinal liquids. The last objective is to investigate their potential as oral conveyance vehicles for curcumin loaded by modified SLN. The novel carrier is made out of a lipid center intended to secure and control the release of curcumin that should encourage the cooperation of the transporter with the intestinal mucosa and the further vehicle of the hydrophobic medication.

## METHODS AND MATERIALS

*Instrument*

Nano-suspension was prepared using the micro-emulsification technique. The following materials were obtained from the indicated sources and used in our study without further purification. Tripalmitin glyceride was purchased from Alfa Aesar (Germany), and palmitic acid from Sigma-Aldrich (St Louis, MO). Polysorbate 20 (Tween 20) and sucrose were obtained from Merck (Darmstadt, Germany). Curcumin purchased from Sigma Company. High-pressure liquid chromatography (HPLC) grade butanol and analytical grade chloroform and ethanol were also purchased from Merck. Other reagents were of analytical or HPLC grade. Double-distilled water was prepared in our laboratory.

The morphology and size of the PEG-SA-SLNs was analyzed by TEM (Zeiss-EM 10C-Germany) at an accelerating voltage of 80 kV fit for highlight point. Prior to examination, the examples were weakened 1:2 and applied on a carbon-coated grid, at that point recolored with uranyl acetate acid derivation for 30s and set on copper g Differential Scanning Calorimetry (DSC) examination of NP components and PEG-SA-SLNs were performed utilizing a Shimadzu DSC-50 outfitted with a Shimadzu warm analyzer TA-50 (Shimadzu, Japan) rids with films for perception. A warming amount of 10°C/min was utilized in the 0°C–300°C temperature extend. The potential interaction between the solid lipid core and incorporated drug was investigated using FT-IR studies (Perkin-Elmer).

Curcumin extracted and extract concentrations were determined using an HPLC system (LC-10AS Liquid Chromatograph, SCL-10A System Controller, SIL-10AV UV-Vis Detector, C-R6A Chromatopac, shimadzu, Japan).

*Preparation of lipid NPs and lyophilization*

Gasco et al. created SLN arrangement methods which depend on the dilution of microemulsions [21, 22]. Both lipid NPs were delivered by the strategy portrayed by microemulsion technique. In brief, NPs were prepared utilizing a hot liquefy Tripalmitin glyceride lipid and palmitic acid, by stacking curcumin at a last grouping of 25 mg/mL. At that point, 0.04 mg of PEG-SA was added to the natural stage containing an emulsifier polysorbate 80, co-emulsifiers (butanol) and water. The hot microemulsion was scattered in cool water (2-3°) under mixing (750 rpm) [21]. Regular volume proportion of the hot microemulsion was balanced 1:10 to water [21]. The SLN mixture was then washed twice with water utilizing a membrane (cut off 10,000–12,000 Da) in ultrasonic cleaning tank due to the deletion of the extent of the surfactant atoms applied for getting the microemulsion [23-25].

Sucrose was utilized in the freeze-drying process as cryoprotectants at a centralization of 3 wt%. The suspension of lipid NPs solidified in a fluid sucrose arrangement at −70 ◦C overnight, and afterward as an example moved to the freeze-dryer (ZiRBuS innovation VaCo 5, D-37539) at −50 ◦C for 72 h, and then SLN powders were gathered for additional trials.

*The stability of lipid NPs in simulated gastrointestinal media*

1% (w/v) of NPs were incubation in HCL medium (0.063M) at pH 1.2. Optical Density (OD) was investigated at λ = 345 nm [13] previously and 1 h after incubation to assess the NPs aggregation and arrangement turbidity. The assessment of the strength of PEG-SA-SLNs and SLNs that incubated in acid solution for 1 h, additionally performed. At that point, NPs were isolated from the medium utilizing centrifugation at 5000 × g for 5 min. The size of NPs in the higher arrangement was estimated by Photon Coloration Spectroscopy (PCS) [20, 21, and 23].

*The feature of lipid NPs*

PCS (Nanotrac Wave II Instruments, UK) was utilized for the assessment of size and zeta potential was estimated by photon relationship spectroscopy (Nanotrac Wave II Tools, UK). Examination of surface morphology of PEG-SA-SLNs was accomplished by scanning electron microscopy (SEM) (SEM, KYKY-EM3200, China).

*Determining Percent Entrapment Efficiency and Drug-Loading Capacity*

The proficiency of drug entrapment and drug loading were inspected by deciding the convergence of curcumin in the supernatant of ultra-centrifuged Nps arrangement. NPs suspension were centrifuged at 15,000 g for 45 min to isolate the unentrapped tranquilize. Supernatant was decanted and assimilation of supernatant arrangement was analyzed by Ultraviolet spectrophotometer at 345 nm (Agilent 8453) [13, 14]. At that point, the amount of free curcumin was accomplished. The curcumin entanglement proficiency and medication stacking of curcumin in the PEG-SA-SLNs and SLNs were considered as follows:

$$EE\ (\%)=\left(\frac{W_a-W_s}{W_a}\right)\times 100 \qquad \text{Eq. 1}$$

$$DL\ (\%)=\left(\frac{W_a-W_s}{W_a-W_s+W_L}\right)\times 100 \qquad \text{Eq. 2}$$

where, EE is entrapment effectiveness, DL is rug loading, and Wa, Ws, and $W_L$ are the heaviness of drug included in the system, broke down weight of drug in the supernatant, and weight of lipid included into the system, separately [24-26].

*In vitro release of curcumin from lipid NPs*

The present investigation which directed by a dialysis bag was for the assessment of the measure of curcumin release [13]. A dialysis bag with a molecular weight cutoff of 12,000 Da was set on diffusion cell. The receptor medium was 50 mL in volume and made out of a fluid arrangement of physiological saline, phosphate cradle arrangement, which blended by an attractive stirrer at 750 rpm to homogenize the medium (pH=7.4). 2 ml of prepared SLNs suspension was poured in the receptor part of diffusion cell. The medium temperature was controlled at 37°C. 2 ml of the phosphate buffer was tacked by a syringe needle and a similar volume of new phosphate buffer was supplanted at certain time spans. The samples were dissected utilizing a spectroscopic technique as depicted beforehand [24, 25, and 27]. The analyses were rehashed multiple times for alleviation of blunders.

*In vitro release kinetics calculation*

In this dissolution study, model-dependent methodologies utilized for correlation of disintegration profiles. In model-dependent methodologies, discharge information was fitted to five dynamic models including the zero-order (Eq. 3), first-order [28] (Eq. 4), Higuchi grid (Eq. 5), Krosmeyer–Peppas [29] (Eq. 6), and Hixson–Crowell (Eq. 7) discharge conditions, so as to find the best fit condition [28, 30]. Zero-order (Eq. 3) data is plotted as a cumulative percentage drug released versus time.

$$C = K_0 tC = K_0 t \qquad \text{Eq. 3}$$

Where C is the concentration, $K_0$ is the zero-order rate constant expressed as concentration/time, and t is time in hours [28-30]. First order (Eq. 4) is obtained by plotting log cumulative percentage drug released versus time [29].

$$\text{Log } C = \text{Log } C_0 - Kt/2.303 \qquad \text{Eq. 4}$$

Where $C_0$ is the initial concentration of the drug, K is the first-order rate constant, and t is the time.

$$Q = Kt^{1/2} \qquad \text{Eq. 5}$$

As per Higuchi's (Eq. 5) data is plotted as cumulative percentage drug released versus the square root of time. Where K is the constant of the system, and t is the time [27].

The mechanism of drug release is evaluated by plotting the percentage of drug released versus log time according to Krosmeyer–Peppas equation. Exponent n indicates the mechanism of drug release calculated through the slope of the straight line. Researchers used the n value for characterization of different release mechanisms, concluding for values for a slab, of $n < 0.5$ for Fick diffusion and higher values of n between 0.5 and 1.0, or $n > 1.0$, for mass transfer following a non-Fickian model [28-30].

$$M_t/M\infty\infty = Kt^n \qquad \text{Eq. 6}$$

Scientists reported that the particle regular area is proportional to the cubic root of its volume, this finding led to derive an equation that can be defined as follows:

$$\sqrt[3]{W_0} - \sqrt[3]{W_t} = K_s t \qquad \text{Eq. 7}$$

Where $W_0$ is the initial amount of drug in the pharmaceutical dosage form, W is the remaining amount of drug in the pharmaceutical dosage form at time t and K is a constant incorporating the surface–volume relation for Hixson-Crowell rate equation [28, 30-31]

## RESULTS AND DISCUSSION

*Preparation of lipid NPs, drug entrapment efficiency, and loading capacity*

A wide range of drugs was fused in SLNs. The essential for getting an adequate loading capacity is an adequately high solvency of drug in the lipid melt. Moderately higher epitome effectiveness comprises one of the significant favorable circumstances of SLNs [14]. For computations of capture productivity and loading capacity, adjustment bends for the bright examines of curcumin led to five arrangements in the focus scopes of $1.3 \times 10^{-3}$ to $1.00 \times 10^{-5}$mol/L; embodiment proficiency and drug loading were 99.00% and 41%, individually. The high ensnarement proficiency of drug is believed to be the consequences of the lipophilic features and high similarity between drug and lipid [23, 25, and 32]. Fig. 1 showed the appearance difference between SLNs loaded by curcumin (a) curcumin (b) in water.

*Characterization of SLNs*

A decrement in zeta potential can be plainly observed because of SLNs adjustment by PEG-SA from - 40 mV for SLNs to - 23 mV for those provided with PEG-SA (Table 1). The nearness of PEG-SA causes a decrease of surface charge. Because the adsorption of steric stabilizers will decrease the zeta potential due to the shift of the

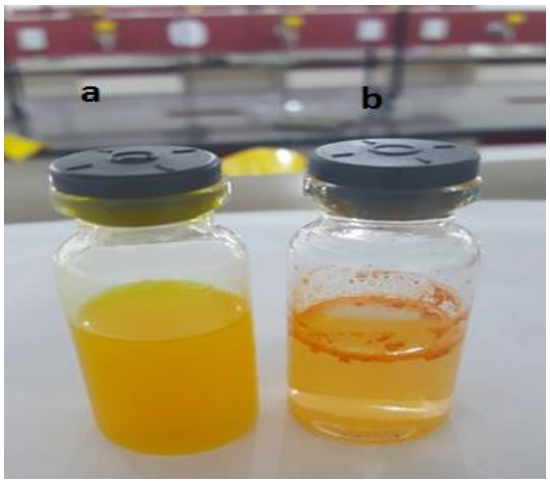


Fig. 1. SLN loaded by curcumin (a) curcumin (b) in water

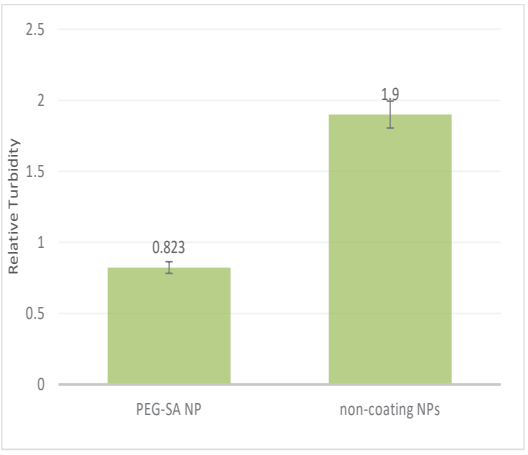


Fig. 2. Relative turbidity of non-coated and surface modified nanoparticles in hydrochloric acid medium (pH 1.2)

Table 1. Size, Poly dispersity index and Zeta Potential of Uncoated SLNs and PEG-SA coated SLNs before and after incubation in acidic medium

| Before incubation in gastric medium | | | | | After incubation in gastric medium | | | |
|---|---|---|---|---|---|---|---|---|
| Formulation | Size (nm) | Poly. index | ζ Potential (mV) | EE(%) | Size (nm) | Poly. Index | ζPotential (mV) | EE(%) |
| SLNs | 153.4±0.01 | 0.182 | -40.0±0.1 | >99 | 219±0.01 | 0.119 | -40.0±0.1 | >99 |
| PEG-SA-SLNs | 176.6±0.01 | 0.196 | -23.0±0.1 | >99 | 198.1±0.01 | 0.260 | -19.3±0.1 | >99 |

shear plane of the particle [33]. The Zeta potential outcomes show that a solid negative charge of SLN surface is incompletely neutralized with coating. As the NPs size is a significant thing for particles to be consumed by the intestinal mucosa, the conglomeration of particles will moderate the availability of intestinal mucosa [27]. The consequences of soundness of the NPs in gastric media show that the low pH of the gastric medium and the pancreatic proteins in intestinal medium are answerable for the genuine conglomeration and degradation of SLNs. In this work, Colloidal drug transporters arranged from strong triglycerides have been introduced as a promising option in contrast to polymer NPs. PEG-SA planned for creating surface changed lipid NPs proposed to embody strong triglycerides inside their structure and to contemplate their physicochemical properties and *in vitro* dependability in gastrointestinal liquids. The last objective is to investigate their potential as oral conveyance vehicles for macromolecules. PEG-SA-SLNs were progressively steady as their polymer covering layer forestalled collection of NPs in gastrointestinal media (acidic medium) [21]. So that research whether pH is an essential role in the accumulation of SLNs recognized in the gastric medium (acidic medium), the solidness of SLNs in an acidic medium (pH 1.2) was estimated by evaluating the turbidity now and again 0 and 1 h post-incubation [21, 23]. SLNs indicated an expansion in turbidity during the examination. No adjustment in turbidity was seen on account of PEG-SA-SLNs (Fig. 2). Likewise, polymer coating prompted abatement in the burst discharge impact because of diminishing the surface association. Following the underlying burst, the systems gave a consistent and moderate arrival of the curcumin [34, 35]. This moderate discharge was credited to the proclivity of the hydrophobic drug for the lipids just as the nonattendance of debasement of the lipid grid under the *in vitro* discharge conditions [21, 36, and 37].

TEM picture of the examples containing drug loaded PEG-SA-SLNs are shown in Fig. 3 where in the particle size of PEG-SA-SLNs are in concurrence with the outcomes got with PCS and SEM. Moreover, the imaging investigations demonstrated that these particles show a circular shape, and a thick lipid matrix without accumulation [18]. The consequences of PCS, TEM and SEM pictures of the PEG-SA-SLNs are introduced in Figs. 3, 4, 5 and Table 1, separately.

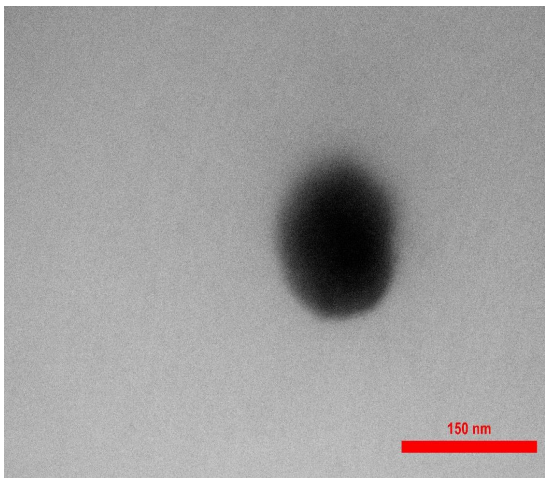


Fig . 3. TEM image of PEG-SA coated Solid lipid nanoparticles.

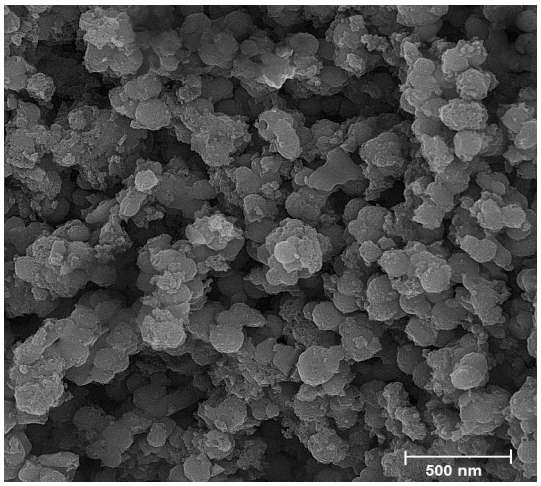


Fig. 4. SEM image of PEG-SA coated Solid lipid nanoparticles (SLNs)

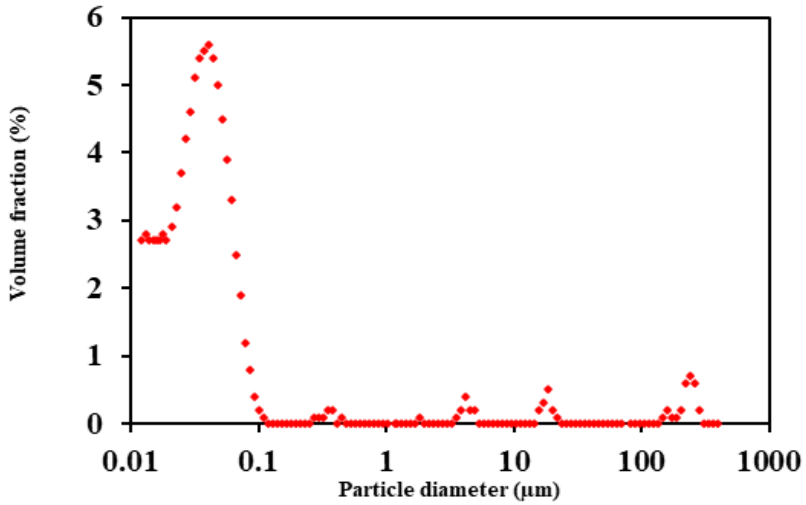


Fig 5. Particle size distribution of PEG-SA coated Solid lipid nanoparticles (SLNs)

TEM and SEM strategies affirm that the NPs are round fit as a fiddle and very much scattered and isolated on a superficial level. The spans of the NPs dictated by PCS are in acceptable concurrence with TEM results. The measurement controlled by PCS is around 150 nm, which is fundamentally the same as the information got by TEM. The normal breadth dictated by the two PCS and TEM was found around 150 nm. TEM pictures affirmed that the NPs were roundabout to ellipsoidal fit as a fiddle with a smooth surface [35-37].

Due to Table 1, the size of SLNs increments after incubation in gastric medium while the PEG-SA-SLNs are pitifully developed [34-36]. This strategy was chosen since it made the exemplification of curcumin plausible. Moreover, the outside of the particles can be altered through the joining of Tween 20 or the lipid derivative PEG-SA into the definition [18]. This alteration prompted a decrease in the zeta likely qualities, shifting from −40 mV for SLNs to −23 mV for those provided with PEG-SA. Consequences of the solidness of the NPs in gastric and intestinal media show that the low pH of the gastric medium and the pancreatic compounds in intestinal medium are liable for the broad collection and corruption of SLNs (80% degradation in 1 h) [18, 23]. Interestingly, PEG-SA- SLNs were increasingly steady, as their polymer coating layer completely forestalled total in the two media and essentially decreased pancreatin-initiated corruption (40% around in 1 h. In the other word, the PEG-SA layer can mostly cover the negative

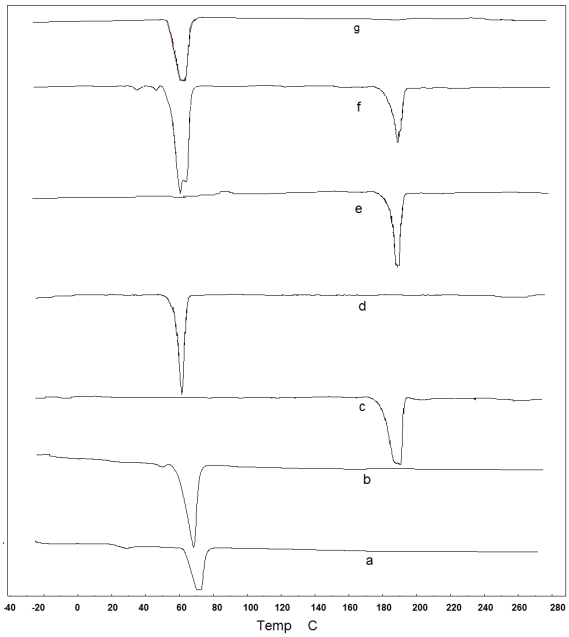


Fig. 6. Differential Scanning Calorimetry thermograms for curcumin, tripalmitin glyceride (a) palmitic acid, (b) PEG-SA, (c) sucrose, (d) tripalmitin glyceride, (e) curcumin, (f) physical blend of for curcumin, tripalmitin glyceride, palmitic corrosive, PEG SA, and lyophilized SLNs are appeared in Figure 4. Curcumin powder had a sharp melting top at 183°C. DSC data did not show the melting peck of curcumin in the lyophilized SLN suspension.

surface charge of NPs [18, 19, and 38]. Besides, from the data of particle size, it may very well be presumed that the obstruction of NPs against total and lipolytic proteins is expanded by diminishing particle size [18, 19, and 34]. DSC thermograms for curcumin, tripalmitin glyceride, physical blend of curcumin, tripalmitin glyceride, palmitic corrosive, PEG SA, and lyophilized PEG-SA- SLNs are appeared in Fig. 6. Curcumin powder had a sharp melting top at 183°C. DSC data did not show the melting peak of curcumin in the lyophilized PEG-SA- SLNs suspension. In any case, we saw the melting peak of curcumin in the physical blend. This recommended curcumin sodium that may be available in an amorphous state.

In FT-IR studies (Fig. 7), Curcumin showed its signature peaks at 3414 $cm^{-1}$ (phenolic O-H stretching vibration), 1625 $cm^{-1}$ (aromatic moiety C=C stretching), 1585 $cm^{-1}$ (benzene ring stretching vibrations), 1512 $cm^{-1}$ (C=O and C=C vibrations), 1428 $cm^{-1}$ (olefinic C-H bending vibrations), 1282 $cm^{-1}$ (aromatic C–O stretching vibrations), 1031 $cm^{-1}$ (C–O–C stretching vibrations) [39]. The peaks at 1293 $cm^{-1}$ and 940 $cm^{-1}$ are corresponding to the in-plane and out-plane bending vibration of the OH group of PA. The symmetric peaks at 719 and 688 $cm^{-1}$ correspond to the swinging vibration of the OH functional group. The peaks appeared at 3430 $cm^{-1}$ are related to the tensile vibrations of alcoholic OH and the peaks at 2918 and 2853 $cm^{-1}$ are related to the tensile vibrations of aliphatic CHs. C=O peaks appeared at 1737 $cm^{-1}$ and the peaks observed at 1180 $cm^{-1}$ are related to C-O tensile vibrations. Long peaks in 2919 and 2878 $cm^{-1}$ are related to the tensile vibrations of alkane CHs. Also, C=O peak is shown at 1737 $cm^{-1}$ and the strong tensile vibrations related to C-O are observed at 1111 $cm^{-1}$ [40, 28].

The FT-IR spectra of NP components and Curcumin NPs are presented in Fig. 7. FT-IR spectra of plain NPs and pure curcumin exhibit no peak shifting and no loss of characteristic functional group peaks. Therefore, our FT-IR analysis detected no interaction between curcumin and solid lipid core, suggesting that curcumin is compatible with the lipid component of NPs as a drug formulation.

The results of high performance liquid chromatographic analysis for the extract (a) and extracted curcumin (b) showed three peaks at specific retention times. The peak of curcumin in the extract samples and the extracted curcumin are

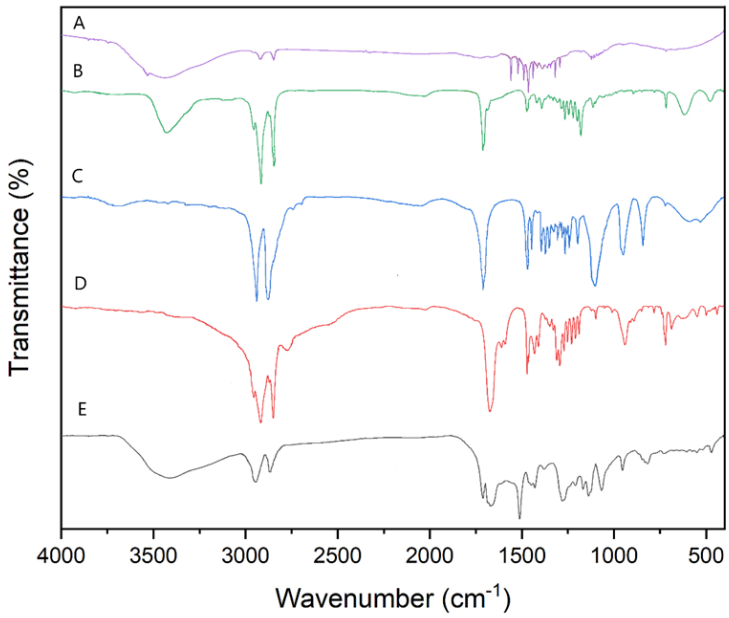


Fig. 7. FT-IR spectra, A: curcumin, B: glycerol tripalmitin, C: palmitic acid, D: curcumin loaded SLN, E: curcumin loaded PEG-SA SLN

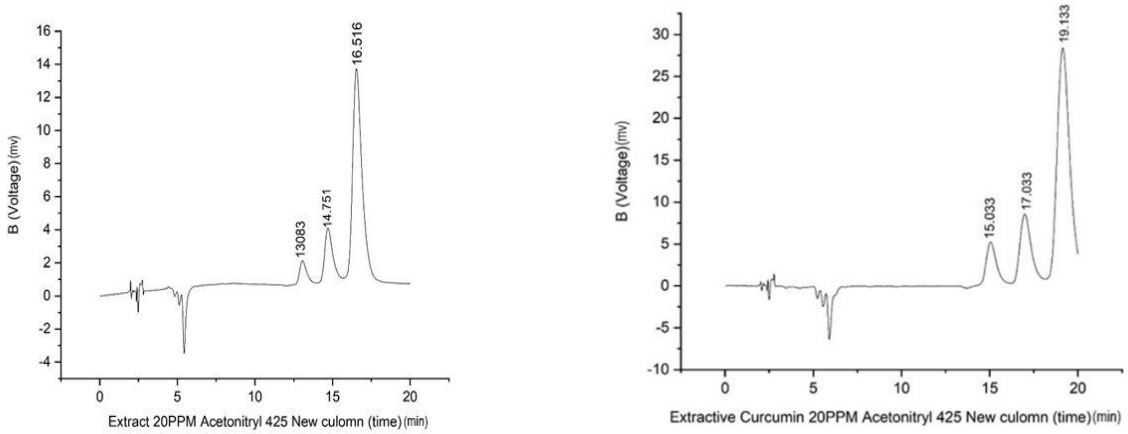


Fig. 8. HPLC chormatograme of curcumin (a) Extract, (b) Extractive curcumin

shown at the retention times of 16 and 19 minutes, respectively. In the study of the area of these peaks, the amount of pure curcumin in the extract was estimated to be 39.8% and the curcumin in the extracted curcumin was estimated to be 81.7%. The results of this analysis showed a 42% increase in the purity of curcumin extract powder compared to the resulting extract (Fig. 8).

*In vitro release characterization*

As it is clear in Fig. 9, contrast of two discharge percent plots of PEG-SA-SLNs and SLNs show the slightest decrease performed for PEG-SA-SLNs because of the coating impact of covering layer [34, 36]. The underlying burst discharge diminishes because of higher thickness of the coated NPs dependent on Fickian diffusion [36, 37]. Covering surface prompts a lessening in the burst discharge impact contrasted with SLNs in light of the fact that the adsorbed curcumin on lipid surface step by step discharges from PEG-SA-SLNs. To be sure, the coating layer obstruction against diffusion of curcumin prompts decrease of drug release.

*In vitro drug release kinetic characterization*

The release data were dissected utilizing the accompanying Higuchi dynamic condition: [30] Regarding the discharge model of PEG-SA-SLNs,

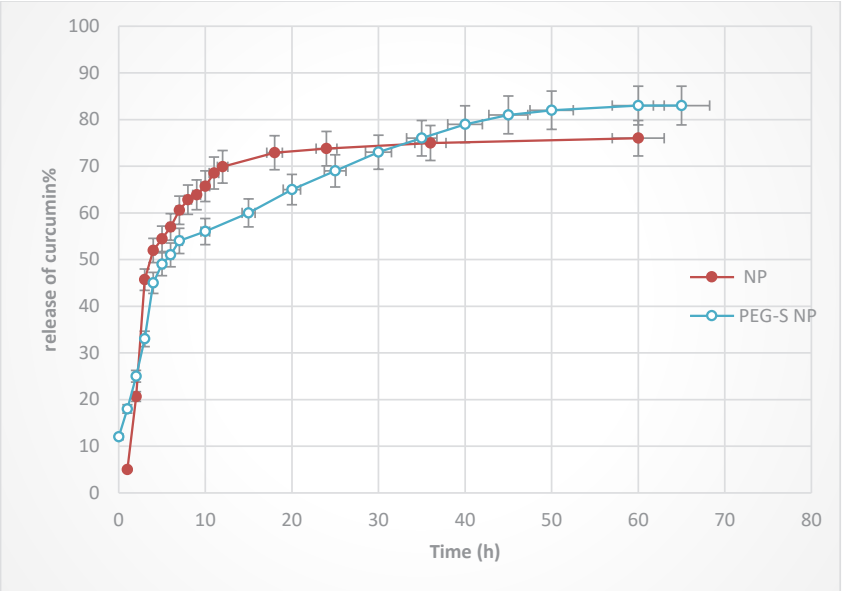


Fig. 9. Release profiles of curcumin from the different lipid nanoparticles: (°) PEG-SA-SLNs (blue line), (•) SLNs (orange line)

Table 2: The $R^2$ values from *in vitro* release kinetics and the K values or release rate constant

| Formulas code | Zero order $R^2$ | First order $R^2$ | Higuchi model $R^2$ |
|---|---|---|---|
| F | 0.938±0.0053 | 0.9643±0.0045 | 0.999±0.0031 |
| K | 0.0546±0.031 | -0.0939±0.021 | 0.01±0.010 |

$R^2$ determination coefficient and k dissolution rate constant ($\mu g ml^{-1} h^{-1/2}$)
Each value represents the mean of three experiments ± SD

it was discovered that the normal drawn out discharge for curcumin was fitted to Higuchi's square root model, as announced for drug loaded PEG-SA-SLNs frameworks [16, 23].

The relapse coefficient ($R^2$) of discharge data of coated NPs acquired by bend fitting technique on different active models is accounted for in Table 2.

Direct fits confirmed that the release profile of curcumin from homogenous and granular matrix systems is dissemination controlled. In view of the $R^2$ value in Table 2, the best information wellness was offered by Higuchi model proposing a dissemination controlled instrument for drug release [34].

## CONCLUSION

The particular point of our work was to grow new lipid NP carriers that may be appropriate for oral administration of hydrophobic medications. Modification of the nanocarrier surface resulted in a reduction in the values of the zeta potential, varying from -0.40 mV for unmodified carriers to -23 mV for modified carriers. These results showed that a strong negative charge of SLN surface is partially neutralized by coating. The results of scanning electron microscopy and transmission electron microscopy showed that nanocarrier is spherical and segregated. The results of DSC confirmed the amorphous nature of curcumin in the nanocarrier and also showed that curcumin has no interaction with other nanocarrier components. The results of high performance liquid chromatography showed that the amount of curcumin in extract and extracted curcumin was obtained in comparison with standard curcumin 39.8% and 81.7%. The encapsulation efficiency of the nanocarrier was high and about 99%. Examination of the release of prepared nanocarrier *in vitro* showed a decrease in the initial explosive release of modified carriers, as well as a slight decrease in the release of curcumin for these carriers due to the coating effect on the nanocarrier surface. The results of stability of

nanocarrier in acidic medium showed low pH as responsible for increasing the size, aggregation and degradation of unmodified lipid nanocarriers. Nanocarriers modified with PEG-SA were more stable due to the polymer coating layer that prevents the aggregation of nanocarriers, so it is possible that PEG-SA reduces the destruction of their lipid nucleus by encapsulating the carriers be in the environment of the stomach and intestines. Studies on the stability of nanocarrier at 25 ± 2 ° C for 9 months in aqueous suspension showed minimal changes in size, polydispersity index, curcumin leakage and changes in appearance.

From the acquired outcomes for drug release, the underlying burst discharge diminishes because of higher thickness of altered NPs dependent on Fickian diffusion. Concerning discharge model everything being equal, it was discovered that the delayed normal discharge for curcumin was well fitted to Higuchi's square root model, as has been accounted for drug loaded PEG-SA-SLNs systems.

## CONFLICT OF *I*NTEREST

The authors declare no conflict of interest.

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