

# The Application of Different Microencapsulation Methods and Formulation Parameters on Antibiotic Loaded PLGA Microparticles for Pulmonary Delivery

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Inhaled anti-infective drugs play a pivotal role in the prophylaxis and treatment of respiratory tract infections. In this study, fluoroquinolone antibiotic levofloxacin hemihydrate-loaded PLGA microparticles were prepared and evaluated. PLGA microparticles were prepared using three different preparation methods such as oil-in-water (o/w), water-in-oil-in-water ( $w_1/o/w_2$ ) and modified water-in-oil-in-water ( $w_1/o/w_3$ ) emulsion solvent evaporation methods. Effects of preparation methods and formulation parameters on physicochemical properties of microparticles characterized in terms of the particle size, encapsulation efficiency, production yield, *in vitro* release and aerodynamic properties were evaluated. Particle size results showed that the increasing volume of dichlorometane in the organic phase caused a significant decrease in particle size of microparticles. Microparticles prepared by using o/w emulsion solvent evaporation method showed a higher encapsulation efficiency value compared to those prepared with double emulsion methods. Biphasic extended-release profile was produced *in vitro*. All formulations prepared except of F1 coded formulation were of suitable aerodynamic size for inhalation having a mass median aerodynamic diameter less than 5  $\mu\text{m}$ . These results showed that levofloxacin hemihydrate-loaded PLGA microparticles could be a potential alternative to the existing levofloxacin therapy in respiratory tract infections.

**Key words:** PLGA microparticles, Emulsification methods, Levofloxacin hemihydrate, Respiratory tract infections, Pulmonary delivery

## Farklı Hazırlama Yöntemlerinin ve Formülasyon Parametrelerinin Pulmoner Veriliş için Antibiyotik Yüklü PLGA Mikropartiküllerine Uygulanması

İnhale anti-enfektif ilaçlar, solunum yolu enfeksiyonlarının teşhisinde ve tedavisinde önemli bir rol oynamaktadır. Bu çalışmada, florokinolon grubu bir antibiyotik olan levofloksasin hemihidrat içeren PLGA mikropartikülleri hazırlanmış ve değerlendirilmiştir. PLGA mikropartikülleri su içinde yağ (y/s), su içinde yağ içinde su ( $s_1/y/s_2$ ) ve modifiye su içinde yağ içinde su ( $s_1/y/s_3$ ) emülsiyon çözücü buharlaştırma yöntemi olmak üzere üç farklı hazırlama yöntemi ile hazırlanmıştır. Hazırlama yöntemlerinin ve formülasyon parametrelerinin mikropartiküllerin partikül büyüklüğü, enkapsülasyon etkinliği, üretim verimi, *in vitro* salım ve aerodinamik özellikleri ile karakterize edilen fizikokimyasal özellikleri üzerine etkileri değerlendirilmiştir. Partikül büyüklüğü sonuçları organik fazda artan diklorometan hacminin partikül büyüklüğünde önemli bir azalmaya neden olduğunu göstermiştir. Tekli emülsiyon yöntemi ile hazırlanan mikropartiküller çoklu emülsiyon yöntemleri ile hazırlanan mikropartiküller ile karşılaştırıldığında daha yüksek enkapsülasyon etkinliği değeri göstermiştir. *In vitro* bifazik uzatılmış salım profili elde edilmiştir. F1 kodlu formülasyon dışında hazırlanan tüm formülasyonlar 5  $\mu\text{m}$ 'den küçük ortalama kütleli aerodinamik çapları ile inhalasyon yolu ile uygulanmaya uygundur. Bu sonuçlar levofloksasin hemihidrat içeren PLGA mikropartiküllerinin solunum yolu enfeksiyonlarının levofloksasin ile tedavisi için bir alternatif olabileceğini göstermiştir.

**Anahtar kelimeler:** PLGA mikropartikülleri, Emülsifikasyon yöntemleri, Levofloksasin hemihidrat, Solunum yolu enfeksiyonları, Pulmoner veriliş

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## INTRODUCTION

One of the most common causes of illness in humans is from respiratory tract infections (RTIs) caused by bacterial, viral or fungal pathogens, all of which have a high cumulative burden of morbidity and economic losses (1, 2). Antibiotics are crucial for the prophylaxis and treatment of RTIs. A major concern with systemic antibiotic treatment of RTIs is the requirement of a high dose to be delivered for effective eradication of the organism (3, 4). Systemic administration of high dose antibiotics comes with a variety of undesirable side effects, including nephrotoxicity and ototoxicity. Hence, in the past decade, the delivery of antibiotics to the lung through inhalation has gained increasing attention in the treatment of pulmonary infections, offering the attractive advantages of delivering high drug concentrations directly to the site of infection, reducing toxicity, and improving the therapeutic potential of existing antimicrobial agents (5). Although aerosol delivery has many advantages, the major challenges faced by localized treatment of RTIs are the rapid absorption and clearance of antibiotics from the lungs and the inability to consistently access the deep lung, where the site of infection usually lies (6, 7). There are very few antibiotic formulations marketed for the treatment of pulmonary infections, e.g. Tobramycin and Aztreonam inhalation solutions for nebulization.

In the last few decades, a great number of studies have focused on developing novel and efficient drug delivery systems to meet different clinical needs (8-11). Polymeric microparticles made of natural and synthetic polymers have shown several advantages as drug carriers, such as high stability both in vitro and in vivo, good biocompatibility, and multifunctionality (12, 13). This potential has been explored for encapsulating antibiotics in polymeric microparticles, which allows slow, sustained release of the drug, improves the pharmacokinetics and biodistribution of antibiotics, overcomes cellular and tissue barriers, and improves the antibacterial efficacy against biofilm-related infectious disease (14, 15). Furthermore, microparticles could be considered proper to provide values

of aerodynamic diameter essential for the particle deposition in the deep lung. Microparticles of mass median aerodynamic diameter (MMAD) 1–5  $\mu\text{m}$ , when inhaled, deposit efficiently in the peripheral lung at the site of pulmonary infection (16).

Poly(D,L-lactide-co-glycolide) (PLGA) has been widely used for the encapsulation and sustained delivery of drugs in the past several years because it is biocompatible, biodegradable, nontoxic and has been approved for several products. PLGA particles are made by many different techniques and have been used to encapsulate, release and deliver various types of therapeutic agents, from low-molecular-weight drugs to macromolecular one (17-22). Particularly, PLGA microparticles have received much attention as a carrier of antibiotics for pulmonary delivery (23-27).

The aims of this study were to prepare and evaluate levofloxacin hemihydrate-loaded PLGA microparticles for pulmonary delivery. PLGA microparticles were prepared using three different preparation methods such as oil-in-water (o/w), water-in-oil-in-water ( $w_1/o/w_2$ ) and modified water-in-oil-in-water ( $w_1/o/w_3$ ) emulsion methods. Effects of preparation methods and formulation parameters on physicochemical properties of microparticles characterized in terms of the particle size distribution, morphology, entrapment efficiency, production yield and in vitro release were evaluated. Also, the aerodynamic properties of microparticles were investigated to determine their suitability for pulmonary delivery.

## EXPERIMENTAL

### Materials

Levofloxacin hemihydrate was kindly supplied by Koçak Farma (Türkiye). Poly(D,L-lactic-co-glycolic acid; PLGA) Resomer<sup>®</sup> RG 504 (50:50 lactic to glycolic acid ratio and a Mw=48 kDa, inherent viscosity 0.56 dl/g) was purchased from Boehringer Ingelheim (Ingelheim, Germany). Poly (vinyl alcohol) (PVA) (88 mole% hydrolyzed, Mw=30 000–70 000) and dichloromethane (DCM) (99.9%, HPLC grade) were obtained from Sigma (Steinheim,

Germany). All other chemicals used were analytical grade.

#### *Preparation of microparticles*

Levofloxacin hemihydrate-loaded PLGA microparticles were prepared by using oil-in-water (o/w) (28), water-in-oil-in-water ( $w_1/o/w_2$ ) (29) and modified water-in-oil-in-water ( $w_1/o/w_3$ ) (30) emulsion methods. In o/w emulsion solvent evaporation method, levofloxacin hemihydrate was added to organic solution of PLGA in DCM. Then, the organic phase was injected into the external aqueous phase consist of 60 mL of 2% (w/v) PVA solution and homogenized by using a high-speed homogenizer (Ultra Turrax<sup>®</sup> T-25, Ika, Staufen, Germany) operating at 13500 rpm for 2 min. In  $w_1/o/w_2$  emulsion solvent evaporation method, the organic solution of polymer was emulsified with an aqueous solution of levofloxacin hemihydrate containing 1% (w/v) Pluronic F-127<sup>®</sup> as a surfactant. In the some formulations, hyaluronic acid was added to the aqueous solution of levofloxacin hemihydrate. This primary emulsion ( $w_1/o$ ) was emulsified with 2% (w/v) PVA solution to form the secondary emulsion ( $w_1/o/w_2$ ). Differently from this,  $w_1/o/w_2$  secondary emulsion was transferred into 300 mL of 0.5% (w/v) PVA solution ( $w_3$ ) and stirred with a mechanical stirrer in modified  $w_1/o/w_3$  emulsion solvent evaporation method. The microparticles were collected by centrifugation (Sigma 2-16P, Germany) at 5000 rpm for 15 min, washed with ultrapure water (MilliQ water) three times and lyophilized to obtain free flowing powder. Before the lyophilized process, microparticles were dispersed within distilled water, frozen at -40°C overnight and placed in the lyophilize equipment (Christ Gamma 2-16 LSC, Canada) operating at 0.05 mmHg during 24 h. Finally, dried microparticles were stored in a desiccator at 25±0.5°C. Compositions used for levofloxacin hemihydrate-loaded PLGA microparticles are shown in Table 1.

#### *Physicochemical Characterization of Microparticles*

##### *Particle size measurement*

The average size of microparticles was measured with a laser diffraction particle size

analyzer (Mastersizer 3000, Malvern Instruments, Germany). Briefly, proper amounts of dry microparticles were mixed with distilled water and suspended completely for several minutes using a vortex. The suspension was then placed in the laser particle counter. The sizes were measured at 25±2°C. Each sample was measured in triplicate.

##### *Morphology of microparticles*

To investigate the shape and morphology of microparticles, they were dispersed in a droplet of water, directly on a slide and observed under an optical microscope (Leica Model DM 4000B, Germany).

##### *Encapsulation efficiency*

Briefly, a determined quantity of levofloxacin hemihydrate-loaded microparticles was first dissolved in 5 mL of DCM. Then, 2 mL of distilled water was added to dissolve the drug completely. The mixture was stirred for evaporation of all DCM at room temperature. The remaining undissolved PLGA was then separated by centrifugation. The clear supernatants were then withdrawn and analyzed for levofloxacin hemihydrate content at 287 nm spectrophotometrically. The encapsulation efficiency (%) was calculated using Equation 1:

$$\text{Encapsulation efficiency (\%)} = \frac{\text{Calculated drug concentration}}{\text{Theoretical drug concentration}} \times 100 \quad (\text{Equation 1})$$

##### *Production yield*

Microparticles recovered at the end of preparation were weighed and the production yield (%) was calculated using Equation 2.

$$\text{Production Yield (\%)} = \frac{\text{Total microparticle amount}}{\text{Total solid material amount}} \times 100 \quad (\text{Equation 2})$$

##### *Thermal analysis for microparticles using the differential scanning calorimeter*

Thermal analysis of levofloxacin hemihydrate-loaded microparticles was performed using a differential scanning calorimeter (DSC) (Shimadzu DSC-60,

**Table 1.** Composition of levofloxacin hemihydrate-loaded PLGA microparticles

Formulation code	Preparation method	Amount of organic solvent (mL)	Amount of drug (mg)	Concentration of hyaluronic acid (%w/v)
F1	w <sub>1</sub> /o/w <sub>2</sub>	2	10	-
F2	w <sub>1</sub> /o/w <sub>2</sub>	3	10	-
F3	w <sub>1</sub> /o/w <sub>2</sub>	4	10	-
F4	w <sub>1</sub> /o/w <sub>2</sub>	3	20	-
F5	w <sub>1</sub> /o/w <sub>2</sub>	3	40	-
F6	w <sub>1</sub> /o/w <sub>2</sub>	3	10	0.25
F7	w <sub>1</sub> /o/w <sub>2</sub>	3	10	0.50
F8	w <sub>1</sub> /o/w <sub>2</sub>	3	10	0.75
F9	w <sub>1</sub> /o/w <sub>3</sub>	3	10	-
F10	o/w	3	10	-

Japan). The samples (about 6.0 mg) were placed in sealed aluminum pans and subjected to heating from 20 to 300 °C at a rate of 5 °C/min. All data obtained were processed on TA 60 universal analyzer software and glass transition temperature (T<sub>g</sub>) was determined.

#### *In vitro release studies*

Microparticle samples were placed into dialysis bags and suspended in 20 mL of pH 7.4 phosphate buffer solution. Then, microparticles were shaken horizontally in a shaking incubator (JeioTech Shaking Incubator Model SI-300, Japan) at 50 rpm and 37±0.5°C. At various time points, samples (1 mL) were withdrawn with a syringe filter (0.45 µm pore size) from the release media, and replaced with an equal volume of the corresponding fresh media. The samples were analyzed at 287 nm spectrophotometrically. The *in vitro* release experiments were conducted in triplicate.

#### *Aerodynamic characteristics of microparticles*

Firstly, the tapped density of the lyophilized microparticles was determined by tapped density measurements using an automatic tapper (Aymes, Turkey) until no further

change in the powder volume was observed. Measurements were performed in triplicate. Theoretical estimates of the particle primary aerodynamic diameter (MMAD<sub>t</sub>) were derived from the particle size and tapped density data, according to Equation 3:

$$\text{MMAD}_t = d (\rho/\rho_0 X)^{1/2} \quad (\text{Equation 3})$$

Where *d* is the geometric mean diameter,  $\rho_0$  is a reference density of 1 g/cm<sup>3</sup> and *X* is the dynamic shape factor, which is 1 for a sphere (31).

#### *Statistical analysis*

Results were expressed as mean±standard deviation (SD) from at least three separate measurements. A one-way analysis of variance followed by post hoc Tukey's multiple comparison test was used to assess statistical difference. All analyses were performed by SPSS for Windows statistical software version 11.5. Significance was established when the *p* value was less than 0.05.

## RESULTS AND DISCUSSION

### Particle size

Particle sizing is an important characterization method to verify the production of microparticles. The laser diffraction technique was used to measure particle size of levofloxacin hemihydrate-loaded microparticles. The values show that the size of the microparticles ranged from  $3.93 \pm 0.12 \mu\text{m}$  (F5) to  $39.6 \pm 5.48 \mu\text{m}$  (F1). Volume of organic solvent plays a critical role in determining the particle size of microparticles. As shown in Table 2, the particle size of microparticles drastically decreased ( $p$  value  $< 0.05$ ) with increasing volume of DCM from 2 mL to 3 mL. While the geometric mean diameter was  $39.6 \pm 5.48 \mu\text{m}$  in the F1 coded formulation prepared with 2 mL DCM, it was  $6.57 \pm 0.34 \mu\text{m}$  in the F2 coded formulation prepared with 3 mL DCM. Considering that, increasing solvent volume caused a decrease in disperse phase viscosity and the production of smaller droplets (32). However, more increasing volume of DCM caused a slight decrease ( $p$  value  $< 0.05$ ) in the particle size of microparticles.

The effect of drug loading on the particle size of the microparticles is shown in Table 2. Increasing the initial weight of levofloxacin hemihydrate dissolved in the inner aqueous phase caused a small decrease ( $p$  value  $< 0.05$ ) in particle size of microparticles.

The particle size of microparticles increased ( $p$  value  $< 0.05$ ) with increasing concentration of hyaluronic acid from 0.25% (w/v) to 0.50% (w/v) in the internal aqueous phase. This may be due to the increase viscosity of internal aqueous phase by adding hyaluronic acid. However, increasing concentration of hyaluronic acid from 0.50% (w/v) to 0.75% (w/v) didn't cause a significant change ( $p$  value  $> 0.05$ ) in the particle size of microparticles.

Levofloxacin hemihydrate-loaded microparticles were prepared by using three different preparation methods. As shown in Table 2, microparticles with similar particle size were obtained when they were prepared by  $w_1/o/w_2$  (F2) or  $w/o$  (F10) emulsion solvent evaporation method. However, a slight decrease in particle size of microparticles was observed when they were prepared by modified double emulsification method ( $w_1/o/w_3$ ).

**Table 2.** Characterizations of levofloxacin hemihydrate-loaded PLGA microparticles.

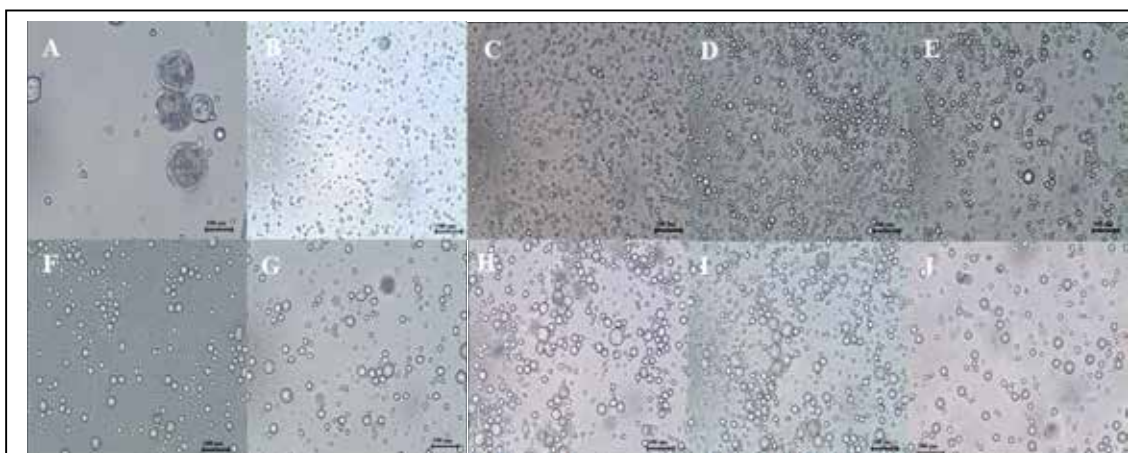
Formulation code	Particle size ( $\mu\text{m}$ ) $\pm$ SD	Encapsulation efficiency (%) $\pm$ SD	Production yield (%)
F1	$39.60 \pm 5.48$	$16.45 \pm 0.03$	90.22
F2	$6.57 \pm 0.34$	$8.95 \pm 0.07$	97.64
F3	$5.47 \pm 0.11$	$8.16 \pm 0.05$	100.00
F4	$4.13 \pm 0.29$	$6.99 \pm 0.09$	89.99
F5	$3.93 \pm 0.12$	$6.94 \pm 0.04$	95.04
F6	$7.15 \pm 0.14$	$10.62 \pm 0.21$	71.97
F7	$9.97 \pm 0.05$	$8.78 \pm 0.15$	71.66
F8	$6.07 \pm 0.04$	$8.93 \pm 0.05$	57.14
F9	$5.34 \pm 0.12$	$10.10 \pm 0.18$	100.00
F10	$6.30 \pm 0.19$	$15.61 \pm 0.03$	71.43

Values are expressed as mean  $\pm$  standard deviation ( $n = 3$ ).

### Particle morphology

Certainly, shape, along with size, is a critical feature of drug delivery particles. The spherical shape is a desirable characteristic for systems to be used as drug delivery device because this allows avoiding the anisotropic swelling normally associated with other geometries (33). The optical microscopy images of levofloxacin hemihydrate incorporated microparticles in Figure 1 demonstrate that the microparticles are spherical shape.

No linear correlation was observed between the encapsulation efficiency values of microparticles and the initial weight of levofloxacin hemihydrate dissolved in the inner aqueous phase. A slight decrease in the encapsulation efficiency was observed when the amount of the levofloxacin hemihydrate increased from 10 mg to 20 mg (Table 2). However, no significant change in the encapsulation efficiency of microparticles was obtained with 40 mg of levofloxacin hemihydrate.



**Figure 1.** Optical microscopy images of levofloxacin hemihydrate-loaded PLGA microparticles. A)F1, B)F2, C)F3, D)F4, E)F5, F)F6, G)F7, H)F8, I)F9 and J)F10.

### Determination of the encapsulation efficiency

The drug encapsulation efficiency of the microparticles is crucial for their clinical application. The encapsulation efficiency of levofloxacin hemihydrate-loaded microparticles ranged from  $6.94 \pm 0.04\%$  to  $16.45 \pm 0.03\%$ .

Table 2 shows that the volume of DCM plays an important role in the drug loading efficiency of microparticles. Increasing volume of DCM from 2 mL to 3 mL caused a significant decrease ( $p$  value  $< 0.05$ ) in the drug loading capacity of microparticles. This may be the result of a decrease in the particle size of microparticles. However, no significant change ( $p$  value  $> 0.05$ ) caused in encapsulation efficiency of microparticles when the volume of DCM increased from 3 mL to 4 mL.

Wu et al. (34) have improved encapsulation efficiency of ofloxacin hydrochloride loaded PLGA microparticles by the addition of hyaluronic acid into internal aqueous phase. This condition could have been caused by the interaction between hyaluronic acid macromolecules and drug. In this study, a slight increase ( $p$  value  $< 0.05$ ) in encapsulation efficiency was obtained when 0.25% (w/v) of hyaluronic acid was added into the internal aqueous phase (Table 2). However, the addition of higher concentration of hyaluronic acid did not cause a significant change ( $p$  value  $> 0.05$ ) in the encapsulation efficiency of microparticles.

Preparation method of microparticles affected drug loading efficiency of microparticles. Comparing with double  $w_1/o/w_2$  emulsion solvent evaporation method, higher encapsulation efficiency value was

obtained when microparticles were prepared by using modified double emulsion ( $w_1/o/w_3$ ) solvent evaporation method. In the  $w_1/o/w_3$  emulsion solvent evaporation method, the solvent diffusion rate was decreased by dividing the double emulsification into two steps and solidifying the droplets step by step. As a result, the emigration of the drug to the external aqueous solution was prevented, thereby retaining more drugs in the internal solution during emulsification (30, 35). Furthermore, encapsulation efficiency values of microparticles increased significantly ( $p$  value $<0.05$ ) when microparticles were prepared by o/w single emulsion solvent evaporation method. Considering that, microparticles prepared by single emulsion method have less porosity compared to those prepared by double emulsion methods (36).

#### *Production yield*

As shown in Table 2, a production yield of range 57.14–100.00% in the microparticle formulations was obtained. Addition of hyaluronic acid to the internal aqueous phase caused a significant decrease in the production yield values of microparticles ( $p$  value $<0.05$ ).

#### *Differential scanning calorimetry measurements*

Thermal behavior of the levofloxacin hemihydrate, PLGA, and levofloxacin hemihydrate-loaded microparticles is shown in Figure 2. The pure PLGA exhibits an endothermic event (48.35°C) referring to the relaxation peak that follows  $T_g$  due to the amorphous behavior of PLGA. Figure 2 illustrates the thermal characteristics of the levofloxacin hemihydrate that it gives a sharp endothermic peak at 235.87°C. This result is in agreement as reported in literature (37). However, there was no evidence of an endotherm related to levofloxacin hemihydrate in the microparticles (F10) possibly because of the conversion of drug substance from crystalline form to amorphous form in polymer matrix.

#### *In vitro drug release evaluation from the microparticles*

To investigate the drug release pattern of microparticles, *in vitro* release studies have

been carried out in pH 7.4 phosphate buffer solution with 0.1% (w/v) Tween 80 at  $37\pm 0.5^\circ\text{C}$ . Because of favorable properties such as particle size and encapsulation efficiency, F10 coded formulation was used for *in vitro* release studies. As shown in Figure 3, microparticles displayed biphasic drug release pattern with a burst release within 1 h, followed by a sustained release afterward. In the first hour, levofloxacin hemihydrate released was 30.89%. The reason for the initial burst in release profile may be due to the levofloxacin hemihydrate associated on and just beneath the surface of microparticles. The slow release in the later stage was attributed to the fact that the solubilized or dispersed drug can only be released slowly from the polymer matrices compared with free drug.

#### *Aerodynamic characteristics of microparticles*

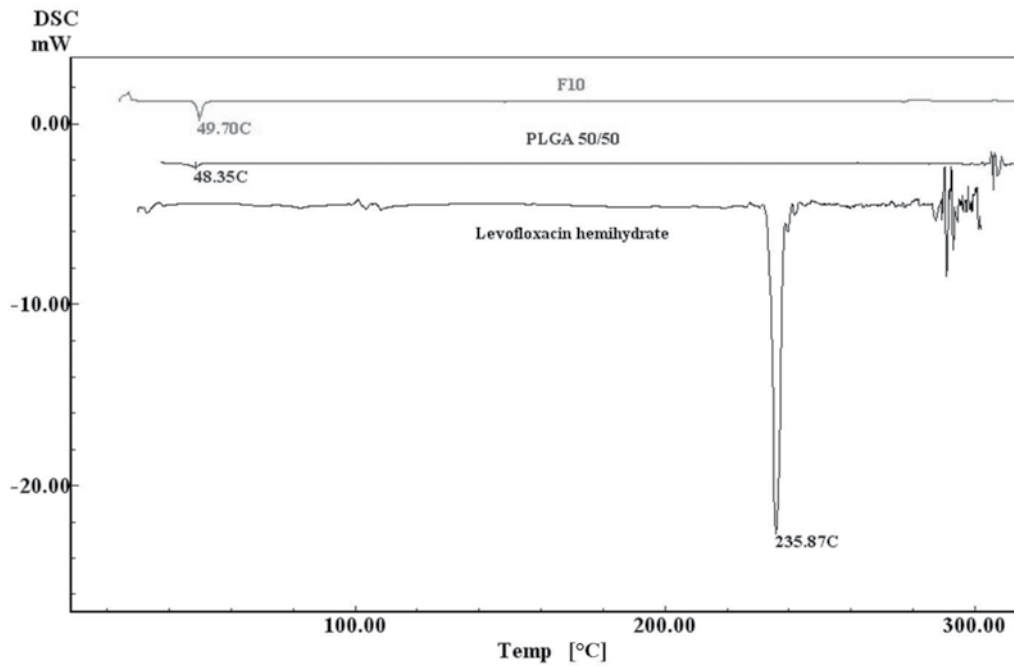
Considering their advantages over other inhalation systems, the inhaler formulation of microparticles was prepared as dry powder inhaler (DPI) system.

The tapped density is an important physical property of dry powders. The tapped density provides significant information about the flow properties of the particles from the inhaler device, the porosity of the particles, the particle size distribution, the true density, and interparticulate cohesive and adhesive forces. A lower tapped density is associated with better aerosolization properties (31). In this study, the tapped density values for the microparticle formulations are found to be  $<0.4\text{ g/cm}^3$  except of F10 coded formulation (Table 3).

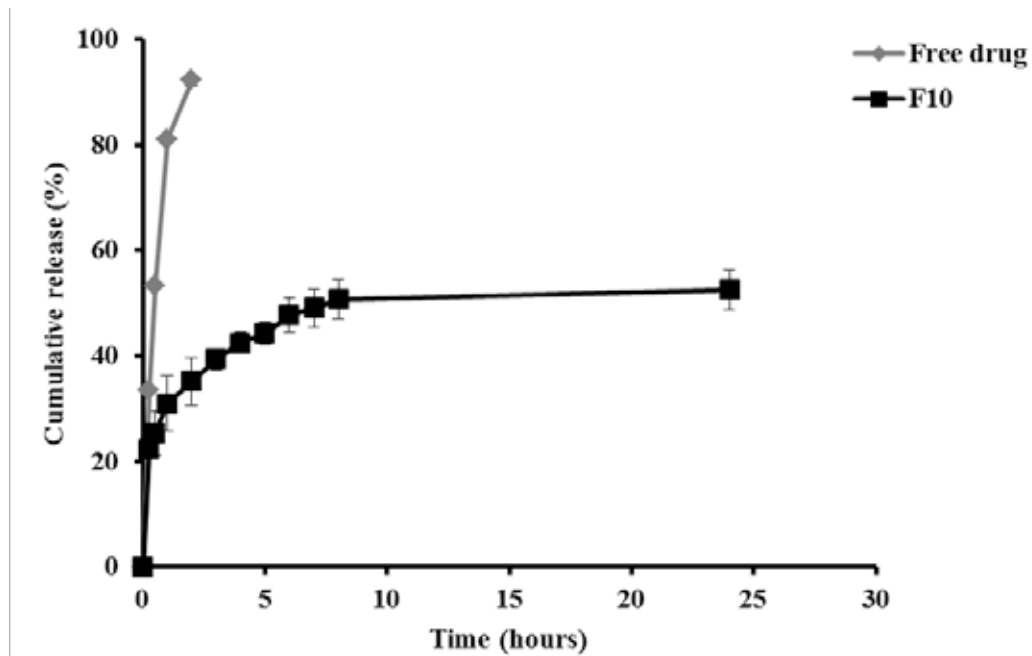
The primary aerodynamic diameter (MMADt) of each formulation calculated from the geometrical particle diameter and tapped density ranged between 2.07 and 18.38  $\mu\text{m}$  (Figure 3), indicating that the all microparticle formulations, except of F1 coded formulation were of a suitable size for deposition in the alveolar region of the lung.

## CONCLUSION

Levofloxacin hemihydrate-loaded PLGA microparticles were prepared by using three different emulsion methods. The type of



**Figure 2.** DSC curves of levofloxacin hemihydrate, PLGA and levofloxacin hemihydrate-loaded PLGA microparticles (F10 coded formulation)



**Figure 3.** *In vitro* release profiles of free levofloxacin hemihydrate and levofloxacin hemihydrate-loaded PLGA microparticles (F10 coded formulation). Values are expressed as mean  $\pm$  standard errors (n = 3).



**Table 3.** Aerodynamic properties of levofloxacin hemihydrate-loaded PLGA microparticles.

Formulation code	Tapped density (g/cm <sup>3</sup> )	MMADt (µm)
F1	0.22±0.013	18.38±0.55
F2	0.32±0.014	3.70±0.08
F3	0.30±0.00	2.99±0.00
F4	0.25±0.00	2.07±0.00
F5	0.33±0.00	2.27±0.00
F6	0.33±0.00	4.13±0.00
F7	0.34±0.00	5.77±0.00
F8	0.34±0.00	3.52±0.00
F9	0.24±0.016	2.63±0.09
F10	0.50±0.00	4.47±0.00

MMADt: Particle primary aerodynamic diameter

Values are expressed as mean ± standard deviation (n = 3).

preparation method and formulation parameters affected physicochemical properties of microparticles. Higher encapsulation efficiency was obtained with o/w emulsion method. In vitro release profile of F10 coded formulation shown that levofloxacin hemihydrate-loaded microparticles exhibited an initial burst followed by a period of slow release. Aerodynamic properties of all formulations except of F1 coded formulation were found to be suitable for pulmonary delivery. The results of our current study showed promising capabilities of levofloxacin hemihydrate-loaded PLGA microparticles for pulmonary drug delivery to treat respiratory infections.

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