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# Preparation and evaluation of a thermosensitive liposomal hydrogel for sustained delivery of danofloxacin using mesoporous silica nanoparticles

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**Key words:**
danofloxacin, drug delivery, liposome, mesoporous silica nanoparticles, thermosensitive

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Received: 18 July 2016
Accepted: 6 September 2016

## Abstract:

**BACKGROUND:** Sustained release delivery system can reduce the dosage frequency and maintain the therapeutic level of drugs for a longer time. Biodegradable, biocompatible and thermosensitive chitosan-beta-glycerophosphate (C-GP) solutions can solidify at body temperature and maintain their physical integrity for a longer duration. **OBJECTIVES:** To develop a novel delivery system based on the integration of liposomes in hydrogel using mesoporous silica nanoparticles (MSNs) for sustained release of danofloxacin in farm animals. **METHODS:** The MSNs were prepared using N-cetyltrimethylammonium bromide and tetraethylortho silica. The liposomes were prepared by thin film hydration method. C-GP solution containing danofloxacin-loaded MSN liposomes underwent different in-vitro tests, including evaluation of the entrapment efficiency, gelation time, morphology, drug release pattern as well as antimicrobial activities against *S. aureus* and *E. coli*. **RESULTS:** The mean pore size of MSNs was 2.8 nm and the mean MSN entrapment efficiency was 45%. Kinetics of danofloxacin release from liposomal hydrogel followed the Higuchi's model. This formulation was capable of sustaining the danofloxacin release for more than 96 h. The FTIR studies showed that there were no interactions between danofloxacin and hydrogel excipients. Scanning electron microscopy (SEM) showed that the formed gel had a continuous texture, while the swelled gel in the phosphate buffer had a porous structure. Microbiological tests revealed a high antibacterial activity for lipomosal hydrogel of danofloxacin-loaded MSN comparable with danofloxacin solution. **CONCLUSIONS:** The liposomal hydrogel solidified at body temperature, effectively sustained the release of danofloxacin and showed in vitro antibacterial effects.

## Introduction

Controlled release parenteral dosage forms of antibiotics have many applications in veterinary medicine since therapeutic levels of antibiotics could be maintained

without the need for repeated injections (Medlicot et al., 2004). Recently, a considerable interest has focused on injectable, in situ forming gel for drug delivery. Hydrogels are three dimensional hydrophilic polymer networks capable of absorbing large amounts of water or biological fluids (Patois et al., 2009). Chitosan is obtained from chitin by alkaline acetylation, and it has many desirable properties including biocompatibility, biodegradability and high safety profile (Chang et al., 2009). The hydrogen bonding in chitosan chains due to the presence of amine and hydroxyl groups causes the chitosan solutions to be highly viscous (Bhupendra et al., 2011). A thermosensitive neutral solution based on chitosan/β-glycerophosphate was first reported by Chenite et al. (2001) and has recently become a major area of research. The neutral solution of chitosan and β-glycerophosphate remains liquid at room temperature but changes into a gel at body temperature (Khodaverdi et al., 2012). The in situ gelation mechanism involves neutralization of ammonium groups in chitosan, and strengthening of hydrophobic and hydrogen bonding between the chitosan chains at elevated temperatures (Chenite et al., 2001).

Since drug-loaded particles are suitable for controlled release and drug targeting, they have also been the focus of research in drug delivery systems. Among them, MSNs offer several attractive features, such as having a large surface area, being easily modified, pore size and volume, as well as being chemically inert and allowing easier functionalization of their surface. All of these features provide better control of drug loading and release profile. MSNs could be administered through parenteral and oral routes (Mohseni et al 2015).

Even though toxicity of silica nanoparticles is a concern, many studies have shown that this concern is not serious. For example, one study has shown that single and repeated intravenous doses in mouse caused no death (Liu et al., 2011).

Liposomes are colloidal vesicular structures of one or more lipid bilayers surrounding an aqueous compartment. A conventional drug injected into the blood stream typically achieves therapeutic level rapidly but keeps this level just for a short duration due to metabolism and excretion. Drug encapsulated by liposomes maintains its therapeutic level for a longer duration as the drug must first be released from the liposomes before being exposed to the metabolism and excretion processes (Shashi et al., 2013).

Danofloxacin, as a third fluoroquinolone antibacterial drug, acts by inhibition of bacterial DNA-gyrase. It has a rapid bactericidal activity against numerous Gram-negative and some Gram-positive bacteria, mycoplasmas and intracellular pathogens like *Brucella* and *Chlamydia* species (Yang et al., 2014). It has also shown excellent activity against respiratory pathogens of cattle, swine and poultry. Among the various drug delivery systems considered for pulmonary infections, nanoparticles have demonstrated several advantages, such as prolonged drug release, cell-specific targeted drug delivery or modified distribution of drugs, both at cellular and organ level (Beck-Broichsitter et al., 2009). For this purpose, MSNs with pore sizes in the range from 1 to 3 nm were synthesized. Due to high water solubility of danofloxacine, drug-loaded MSNs were encapsulated in liposomes and then added to chitosan/β-GP hydrogel. The release behavior of liposomal hydrogel containing danofloxacin-loaded MSNs as well as its

morphology, gelation time and antibacterial activities were studied.

## Materials and Methods

Medium molecular weight chitosan, with a degree of deacetylation (DDA) of 75-85% and β-Glycerophosphate disodium salt pentahydrate, were purchased from Sigma-Aldrich Chemical Co. (St. Louis, USA). Cetyltrimethylammonium bromide (CTAB, 98%) was purchased from Merck (Darmstadt, Germany). Tetraethyl orthosilicate (TEOS, 99%), egg phosphatidil choline and cholesterol were purchased from Sigma Aldrich (Seelze, Germany). Danofloxacin mesylate was provided by Kimiafaam Pharmaceutical Co. (Tehran, Iran). Acetic acid was purchased from Merck. All other chemicals were reagent grade.

**Synthesis and characterization of MSNs:** At first, N-cetyltrimethylammonium bromide (CTAB, 1.00 g, 2.75 mmol) was dissolved in 480 ml of deionized water, and then, 3.5 ml of NaOH (2.0 M) was introduced to the CTAB solution at 80 ºC. After increasing the temperature to 80 ºC, TEOS (5 mL, 21.9 mmol) was added drop-wise at a rate of 1mL/ min to the previous solution. The reaction mixture was stirred vigorously at 80 ºC for 2 h. The white precipitate was isolated by filtration. Nanoparticles were washed with water and methanol and then dried under vacuum at 80 ºC for 24 h. The surfactant was removed via calcination of the obtained powder. The powder was heated to 540 ºC with a heating rate of 1 ºC/min and then at 540 ºC for 4 h. The surface area and pore size of MSNs were determined using a N2 adsorption-desorption instrument (Quanta chrome NOVA Automated Gas Sorption System, 2000e, USA).

**Development of liposomes containing danofloxacin-loaded MSNs:** Prior to liposome fusion, MSN (100 mg) was incubated with danofloxacin in 5.0 mL of water (10 mg/mL) for 24 h at room temperature. After stirring for 24 h under light-sealed conditions, the danofloxacin-loaded MSNs were centrifuged and washed with 20 mL of acetonitrile. To evaluate the danofloxacin loading efficiency, the supernatant was collected, and the residual danofloxacin content was determined by a UV spectrophotometer at 276.8 nm. The loading capacity of danofloxacin (Dano) was calculated by the following equation:

Loading capacity (%) = [(initial Dano (mg)- Dano in supernatant (mg)) / weight of formualation (mg)] * 100

The liposomes were prepared by a lipid-film based method (Sharma, 1997). Briefly, 50 mg of L-α-PC (phosphatidyl choline) and 10 mg of cholesterol were dissolved in 5 ml of chloroform and evaporated to form a thin lipid film with a rotary evaporator. Then, the formed lipid film was re-hydrated in 10 ml of distilled water prior to loading the danofloxacin in MSNs and was sonicated for 15 min. Finally, the mixture was centrifuged at 10,000 rpm for 30 min.

**Preparation of hydrogel:** Chitosan powders (250 mg) were dissolved in 6 ml of 0.1 M acetic acid and were gently stirred for 3 h to make a homogeneous solution. Then liposomes were fused with the chitosan solution and stirred for another 1 h. To make the β-GP solution, 1000 mg of β-GP was dissolved in deionized water. The chitosan and β-GP solutions were placed separately in an ice-water bath at 4 ºC for 15 minutes. Then the β-GP solution was added drop-wise to the chitosan/liposome solution and stirred for 30 min.

**Determination of gelation time:** In the present study, gelation time was assessed using the inverted tube test, as described by Gupta and coworkers (Zhou et al., 2011). When a test tube containing a solution is titled, it is defined as a sol phase if the solution is deformed by the flow, or a gel phase if there is no flow. Firstly, 2 ml of the chitosan/ β-GP solutions was maintained for 12 h at 4ºC in 5 ml vials with inner diameters of 10 mm to remove air bubbles. The vials were then incubated in a temperature-controlled bath. The sol-gel transition time was determined by inverting the vials horizontally every minute. The time at which the gel did not flow was recorded as the gelation time.

**Standard calibration curve of danofloxacin:** To construct the calibration curve, the danfloxacin solutions were prepared in a phosphate buffer, with a pH of 7.4, at a concentration range of 2.5 - 15.0 µg/ml. The absorbance of the solutions was measured at 276.8 nm using a UV-Vis spectrophotometer (Fig. 1).

**In-vitro drug release study:** The release profile of danofloxacin loaded in MSNs was investigated in phosphate buffer solution (PBS) as the test medium. Accurately weighed amounts of the prepared sample (1.0 g) were used under sink conditions at 37 ºC. At predetermined time points up to 168 h, 1 ml of the release medium was collected and replenished with fresh buffer phosphate. The collected samples were analyzed with a UV spectrophotometer. The amount of the released drug (mg) was calculated by comparing its absorbance, at 276.8 nm, to the absorbance of a 10 mg/ml solution of danofloxacin in PBS. All measurements were performed in triplicate. Data are reported as means ± SD.

**Morphological study:** To maintain the porous structure of the hydrogels, they were freeze-dried first and then SEM was performed. The samples were plunged in liquid nitrogen, and the samples were cut with a cold knife. They were mounted on the plate base and coated with platinum-gold for SEM imaging, at 30 kV, using a scanning electron microscope (FESEM, Hitachi. S4160, Japan).

**FTIR spectra analysis:** The chitosan, β-GP, and dried chitosan/β-GP gel were placed in KBr pellets (the samples were mixed with KBr, with a ratio of 1:100, and pressed to form pellets) and were studied using an FTIR spectrophotometer (Nicolet, Model Impact 410; Madison, WI), in the range of 400-4000 cm-1 and at room temperature.

**Microbiological tests:** To determine the antibacterial activity of danofloxacin liposome hydrogel, the well diffusion test was carried out using *Escherichia coli* (*E.coli*) ATCC10145 as a Gram-negative pathogenic strain and *Staphylococcus aureus* (*S. aureus*) ATCC29213 as a Gram-positive pathogenic strain. The bacterial suspensions with a cell density of 0.5 McFarland (1.5 $\times 10^8$ CFU/ml) were transferred onto the surface of Muller-Hinton agar plates using sterile cotton swabs. Wells with diameters of 8 mm were prepared by punching a sterile cork borer onto the solid agar medium. Aliquots (20 µl) of the danofloxacin gel (containing 20µg/ml of the drug) for danofloxacin hydrogel, danofloxacin suspension as positive control, the blank preparation (formulated exactly in the same way as the drug formulation but without adding danofloxacin) as a control to investigate the antimicrobial properties of chitosan and other ingredients were poured into the wells. The

plates were kept for 30-60 min in an upward position to facilitate the distribution of the formulations in the media. After incubation for about 24 h, at 37 °C, the zones of inhibition around the wells were measured in mm using a caliper. All experiments were carried out in triplicate (Jahangirian et al., 2013).

## Results

**In-vitro drug release:** As shown in Fig 2, a prolonged release pattern was observed for danofloxacin. About 27% of the drug was released within 24 h from the formulation and nearly 70% of the loaded drug was released within 96 hours. No burst effect was seen.

The release kinetic pattern of the drug from the prepared hydrogel was analyzed and the best method for this formulation was determined using a regression coefficient ($r^2$) close to 1. The values for $r^2$ were: Zero Order model, 0.90701; First Order model, 0.6645; Higuchii model, 0.9827; Hixon-Crowell model, 0.8339 and Korsmeyer-Peppas, 0.7574. According to the regression coefficient values, the drug release data best fit with Higuchi's kinetic model.

The most familiar form of Higuchi's model is the simplified Higuchi model, which relates drug concentration to the square root of time:

$Mt^{gel}=kHt^{1/2}$

where $Mt^{gel}$ is the concentration of the drug in the drug matrix at time t and KH is the Higuchi dissolution constant (Singhvi et al., 2011)

**Gelation time:** The gelation process of liposomal hydrogel formulation was temperature- and time-dependent. By raising the temperature, the gelling process accelerated; by increasing the temperature from 32 to 37°C the solidification time of the hydrogel was reduced from 30 to 15 min, and above 37°C, increasing the temperature did not change the time of gelling. The sol to gel transition at room temperature is illustrated in Fig 3.

Table 1. In-vitro antibacterial activity of danofloxacin gel and danofloxacin solution as positive control (20μg/ml) against *S. aureus* and *E. coli* bacteria. * Data are expressed as mean ± standard deviation, n=3.

| Bacteria | Zone of inhibition (mm) | |
|---|---|---|
| | Danofloxacin gel | Control positive |
| *S. aureus* | 29.0±0.5 | 32.0±4.5 |
| *E. coli* | 36.0±1.0 | 40.0±2.9 |

**Fourier transform infrared spectroscopy (FTIR) studies:** The FTIR spectra of the lyophilized chitosan, β-GP, chitosan/β-GP, danofloxacin and liposomal hydrogel immediately after the gelation showed that there were no interactions between danofloxacin and excipients.

In the range of 2850- 2950 $cm^{-1}$, the spectrum of chitosan has one asymmetric band, at 2923 $cm^{-1}$. This band probably consists of two overlapping bands which represent the stretching vibrations in the aliphatic groups (-CH2 and -CH3) which are characteristic of the pyranose ring of chitosan.

The spectrum of chitosan shows a band at 16503 $cm^{-1}$ which is assigned to the C=O stretch of the amide bond and at 1595 $cm^{-1}$ which is assigned to the NH2 group of chitosan. These bands indicate that chitosan is a partially deacetylated product of chitin. In this range of frequency, no significant changes were observed.

In the range of 1200- 1500 $cm^{-1}$, the chitosan molecule showed four peaks, with the bands being 1255, 1315, 1380 and 1423$cm^{-1}$. The bands at 1423 and 1315 $cm^{-1}$ are associated with the oscillations characteristic of C-H bending of CH2 groups. The band at

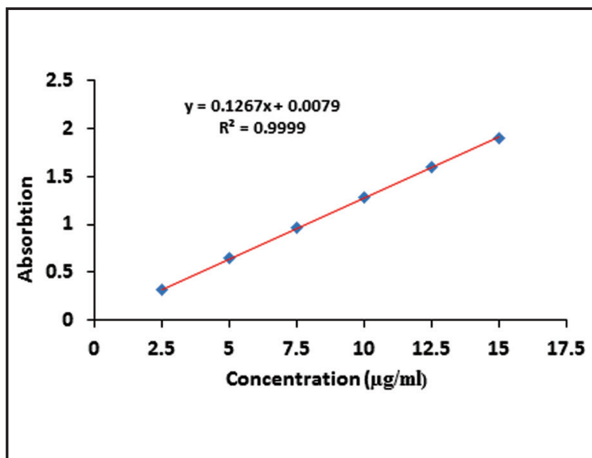

Figure 1. Calibration curve of danofloxacin in the phosphate buffer.

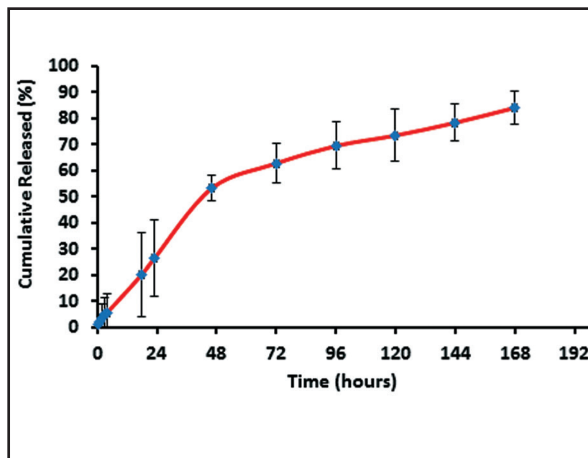

Figure 2. In vitro drug release profile of danofloxacin from the hydrogel.

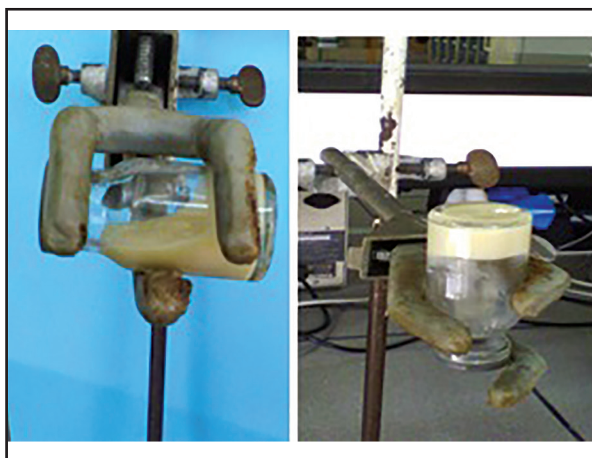
Figure 3. The chitosan/GP formulation at room temperature (left) and at 37°C (right).

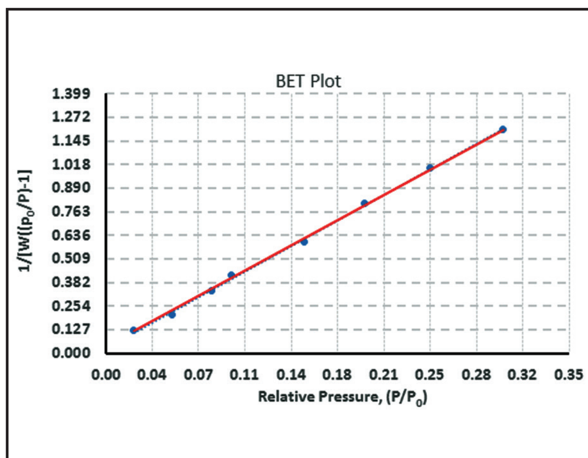

Figure 4. BET plot of the prepared MSNs.

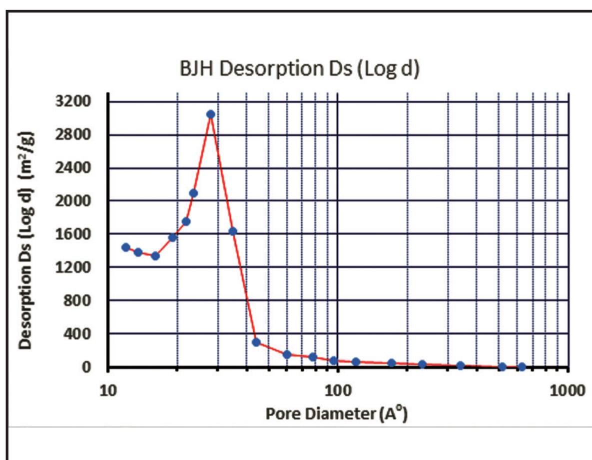

Figure 5. Pore size distribution of the prepared drug-free MSNs.

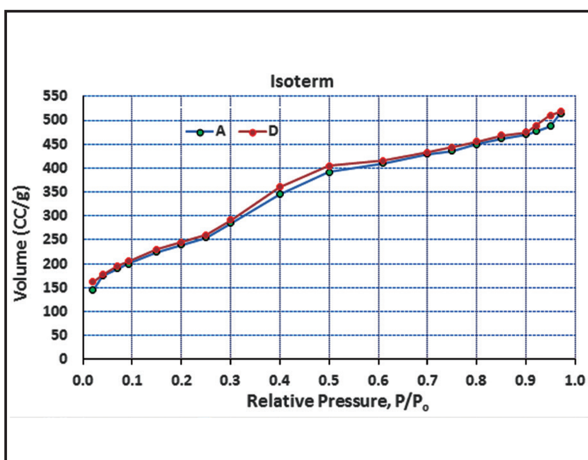

Figure 6. Nitrogen adsorption (A)/desorption (D) isotherm of the prepared MSNs.

1380 $cm^{-1}$ represents the C-O stretching of the primary alcoholic group -CH2-OH.

In the wave length range of 800- 1200 $cm^{-1}$, the FTIR spectrum of chitosan showed three bands at 894,1030 and 1155 $cm^{-1}$. The wide band at 1030-1155 cm-1 represents the

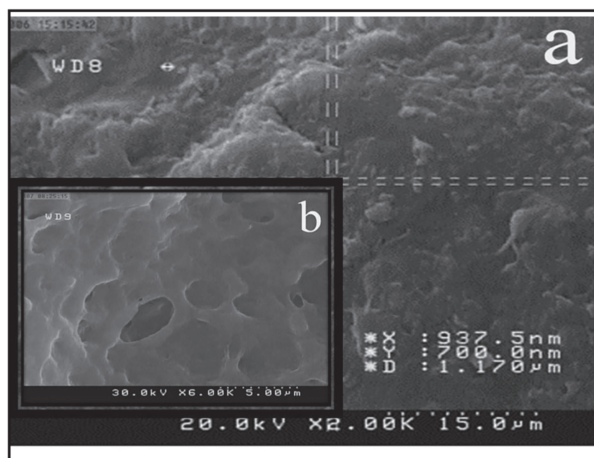


Figure 7. SEM of freeze-dried liposomal hydrogels (a) and swelled hydrogel in the phosphate buffer (b).

bridge C-O-C stretch of the glucosamine residues.

Two characteristic bands of GP appear at 976 $cm^{-1}$ and 1069 $cm^{-1}$; the band at 976 $cm^{-1}$ indicates aliphatic P-O-C stretching; the band at 1069 $cm^{-1}$ is characteristic of the -PO42- group and the band at 920 $cm^{-1}$ may indicate the presence of the -HPO42- group. The FTIR spectrum of the chitosan/β-GP system after the gelation indicates char acteristic bands for chitosan and glycerol phosphate disodium salt and there were no additional bands. For the chitosan/β-GP system, the bands of chitosan at 1380 and 1315 $cm^{-1}$ were shifted to 1385 and 1319 $cm^{-1}$, respectively and the bands of GP at 1076 and 971$cm^{-1}$ were shifted to 1069 and 976 $cm^{-1}$. No significant differences were seen on the FTIR spectra between the hydrogel and those of the danofloxacin, chitosan and β-GP.

**Nanoparticle characterization:** The Brunauer- Emmett- Teller (BET) surface areas and the BJH pore size distributions for NH2-MSN are shown in Fig. 4 and Fig. 5. The BET curve for MSN exhibited type-IV adsorption-desorption isotherm pattern according to IUPAC nomenclature for porous samples. The BET surface area for MSN was found to be 890.54 $m^2/g$. The BJH pore size distributions for MSN showed 2.8 nm (Fig 5). The porous nature of the MSN was confirmed using nitrogen adsorption-desorption isotherms plot (Fig 6).

**Morphology:** The SEM photograph of the liposomal hydrogel shows that the formed gel had a rough and non-porous surface, while the swelled hydrogel in the phosphate buffer (pH=7) had a porous structure, as shown in Fig 7.

**Antimicrobial activity:** The antibacterial activities of the danofloxacin hydrogel and danofloxacin solution as diameter of their zones of inhibition against *S. aureus* and *E. coli* are shown in Table 1. No inhibition zone was observed for the gel without danofloxacin (the blank preparation).

## Discussion

The aim of this study was to prepare a novel formulation of danofloxacin as a third generation fluoroquinolone antibacterial drug for sustained release drug delivery in veterinary medicine. In the present study on drug release, there was no prominent burst effect and the pattern of the release showed a smooth and sustained release with 27% and 53% of the cumulative in-vitro drug being released by the end of 24 and 48 h, respectively, although the release continued with a lower rate up to 168 h (85%). Regarding the kinetics of drug release and according to regression coefficient values, the drug release from the formulation was best fitted to Higuchi's kinetic model. This sustained release parenteral dosage form could be desirable for farm animals because it demonstrates minimized need for repeated injection, more compliance on drug therapy with promisingly better pharmacokinetic profile

and antimicrobial efficacy in comparison to conventional dosage forms.

The injectable liposomal hydrogel has opened up a novel line of research in the field of minimally invasive and in situ forming gels as it can sustain the release of low-molecular weight hydrophilic drug-like danofloxacin for more than 96 h. Moreover, the system is biodegradable, biocompatible, and devoid of surfactants, and it shows minimal mechanical irritation upon in vivo implantation because of its soft and elastic nature. This type of formulation was prepared for cytarabine to reduce dosage frequency and sustain drug action (Mulik et al., 2009). It was capable of maintaining the therapeutic serum levels of cytarabine for more than 60 h. Thirumaleshwar et al. (2012) also designed a liposomal hydrogel as a wound dressing to provide an effective barrier to prevent the infection of the wound and further progression of infection to deeper tissues. Khaled et al. (2010) prepared an ocular prolonged-release liposomal hydrogel containing ciprofloxacin which effectively increased the ocular bioavailability of ciprofloxacin.

Drug release rate can also be controlled by functionalization of MSNs. For example, the release of vancomycin from cadmium sulfide (CdS) capped mobile crystalline material 41 (MCM-41) type MSNs was shown to be extended for up to 3 days and the loading and release mechanism of the MSN system was based on the capping and uncapping of the openings of the mesopores with CdS nanoparticles (Lai et al., 2003). A controlled release of captopril using MCM-41 showed enhanced release profile upon silylation and it is suggested that the drug release profile can be controlled by tailoring the surface properties and pore size (Qu et al., 2006). Amine functionalized Santa Barbara-type mesoporous particle-15 (SBA-15) MSNs' release of tetracycline (TC) was shown to be extended up to 48 h and the TC-MCM-41 nanoparticles were more efficient than the free TC against *E. coli* in culture over a period of 24 h (Hashemikia et al., 2015). Thus, drug release could potentially be extended from our materials through surface functionalization.

In this study, the solidification of the liquid hydrogel was time- and temperature-dependent. All samples had the same gelation time above 37°C, lasting for about 15 min. By increasing the temperature from 32 to 37°C the gelation process was accelerated. It seems this process occurs via the creation of junction zones of the polymers mainly with changes in attractive versus repulsive forces like electrostatic repulsion between chitosan chains and strong chitosan-water interactions. These interactions were as a result of the polyol part of glycerophosphate which protects the chains against aggregation at low temperature. By increasing the temperature, chitosan chain polarity is reduced, protons from chitosan amine groups transfer to the phosphate moiety of glycerophosphate, sheets of water molecules around chitosan chains are removed and consequently attractive interchain hydrophobic and hydrogen bonding forces are strengthened to form hydrogel (Chenite et al., 2001).

Ruel Gariepy et al. (2002) reported that thermosensitive chitosan-beta-glycerophosphate (C-GP) solution containing loaded liposomes remained in sol state at 8-15°C and turned into a gel at body temperature after SC/IM injection. This system is reported to be able to sustain the drug release for more than 2 weeks. The major advantage of com-

bining liposomes with the C-GP hydrogel system is the more sustained release of the drug along with overall stability compared with liposomal suspension. Moreover, this formulation offers some advantages over other systems. Zentner et al. (2001) reported that the onset of gelation of PLA- PEG-PLA was at 14°C and the transition to the solid-like gel state was complete around 18°C; this transition temperature which is very close to room temperature complicates handling of the preparation but our formulation remains liquid at room temperature for several hours and thus is easily injectable.

One of the main objectives of the current study was to prepare MSNs with an increased specific surface area and pore volume in order to achieve high loading of drug molecules. The chosen MSNs presented a high surface area and good pore volume, prior to the loading studies. Passive loading was chosen as the preferred method to load drug molecules and to increase the loading efficiency. In this study, the mean loading efficiency was about 45%. Hashemikia et al. (2015) reported TC loading in SBA-15 type MSNs as 42.3% w/w.

Among the factors affecting the loading process is the polarity of the organic solvent (Charnay et al., 2004). The chosen solvents were deionized water with a polarity index of 10.1. Since the interaction between water and silica nanoparticles prevents the loading process, a better choice may be methanol with a polarity index of 5.1. In addition, time and temperature also influence the loading process and should be further investigated.

The microbiological study showed an effective inhibitory property of this formulation on both Gram positive and Gram negative bacteria. The results showed that the inhibition zones of danofloxacin solution (positive control) were slightly greater than those of danofloxacin hydrogel. This may be due to the fact that the drug was not completely released within 24 hours and therefore produced lower danofloxacin concentrations in this in vitro test.

No drug delivery system is faultless, and this is the case with liposomal hydrogel as well. The cost of this drug delivery is high because of high costs associated with the raw materials as well as expensive equipment needed to increase manufacturing. Another issue is complication with sterilization of liposomes. As they are sensitive to high temperature, it is better for the initial solutions to be filtered through 0.45 μm and thereafter the entire production process to be performed under aseptic conditions (New, 1990).

**Conclusion:** In the present study, the liposomal hydrogel was solidified at body temperature with an appropriate gelation time. This promising formulation was capable of sustaining the release of danofloxacin for more than 96 h and showed suitable in vitro antibacterial effects. Although most novel antimicrobial drug delivery systems are currently in preclinical stages, with ongoing efforts in this field, nanoparticle-based drug delivery systems will improve the practice of antimicrobial therapy in veterinary medicine.

## Acknowledgments

We would like to thank Tehran University of Medical Sciences and University of Tehran for supporting this work. Also, the authors are grateful for the support of Kimiafaam Pharmaceutical Co. (Tehran, Iran) for providing danofloxacin as a gift.

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مجله طب دامی ایران، ۱۳۹۵، دوره ۱۰، شماره ۴، ۳۰۵-۲۹۵

# تهیه و ارزیابی یک هیدروژل لیپوزومی حساس به حرارت برای دارورسانی آهسته رهش دانوفلوکساسین با استفاده از نانوذرات سیلیکای مزوپوروس

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(دریافت مقاله: ۲۸ تیر ماه ۱۳۹۵، پذیرش نهایی: ۱۶ شهریور ماه ۱۳۹۵)

## چکیده

**زمینه مطالعه:** سامانه‌های دارورسانی آهسته رهش می‌توانند دفعات تجویز را کاهش داده و عیارهای درمانی دارو را برای مدت‌های طولانی‌تر حفظ نمایند. محلول‌های زیست تخریب پذیر، زیست سازگار و حساس به حرارت کیتوزان- بتا گلیسروفسفات در دمای بدن ژله‌ای شده و برای مدت طولانی قادر به حفظ یکپارچگی خود می باشند. **هدف:** ساخت یک سامانه دارورسانی جدید آهسته رهش دانوفلوکساسین بر پایه ترکیب لیپوزوم و هیدروژل با استفاده از نانوذرات سیلیکا برای مصرف در حیوانات مزرعه می‌باشد. **روش کار:** نانوذرات سیلیکای مزوپوروس با استفاده از ستیل تری متیل آمونیوم و تترا اتیل اورتوسیلیکا و لیپوزوم‌ها به روش هیدراسیون لایه نازک تهیه شدند. محلول‌های کیتوزان-بتا گلیسرو فسفات حاوی لیپوزوم های دانوفلوکساسین بار شده در نانوذرات سیلیکا تحت ارزیابی‌های مختلف از جمله الگوی رهایش دارو، زمان ژله‌ای شدن، میزان بارگیری در نانوذرات، ریخت شناسی و آزمایشات فعالیت ضدمیکروبی علیه استافیلوکوکوس اورئوس و اشریشیا کلای قرار گرفتند. **نتایج:** میانگین اندازه حفرات نانوذرات ۲/۸nm و میانگین کارآیی بارگیری دارو در نانو ذرات ۴۵٪ بود. کینتیک رهایش دارو از مدل هیگوشی پیروی کرده و قادر به رهایش دانوفلوکساسین به مدت بیش از ۹۶ ساعت بود. براساس مطالعات انجام شده هیچ برهمکنشی بین دانوفلوکساسین و سایر اجزا ژل وجود نداشت. میکروسکوپ الکترونی نگاره ساختار یکنواخت و غیرمتخلخلی را برای ژل نشان داد، در حالی که ژل متورم شده در بافر فسفات دارای ساختار متخلخل بود. آزمایشات میکروبی فعالیت بالای ضدباکتریایی هیدروژل لیپوزومی دانوفلوکساسین و قابل مقایسه با محلول دانفلوکساسین را نشان داد. **نتیجه‌گیری نهایی:** هیدروژل لیپوزومی دانوفلوکساسین در دمای بدن جامد شد و بخوبی قادر به آهسته رهش کردن دارو و نشان دادن اثرات ضدباکتریایی در محیط آزمایشگاهی بود.

**واژه های کلیدی:** دانوفلوکساسین، دارورسانی، لیپوزوم، نانوذرات سیلیکای مزوپوروس، حساس به حرارت

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