Supplementary Material (ESI) for Lab on Chip
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Supporting Information

Nanosized drug formulations under microfluidic continuous flow

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Materials and Methods:

Meloxicam,4-hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carbox-amide-1,1-dioxide (Fig.1) is a nonsteroidal anti-inflammatory drug (NSAID). Meloxicam BP was purchased from Dayang Chemical, Hangzhou, China, and was used as received. Poloxamer 188 was purchased from BASF, Germany, and used as received.

A micro fluidic continuous flow rotating tube processor has been used to prepare the drug nanopartciles. A set flow of liquids were introduced from a conical inlet at one end of the tube, with the discharged liquid collected by a peripheral ring at the other end. Three components were used, meloxicam, organic solvent (benzyl alcohol) and surfactants (Poloxamer 188). Integrated feed pumps were used to deliver the drug dissolved in a solvent, and antisolvent, with and without the addition of poloxamer (in water), with flow rates at 0.3 ml/s and 0.6 ml/s respectively. An organic phase (benzyl alcohol) containing meloxicam was emulsified at different stirring rate of 500 rpm- G force: 16.8 g, 1000 rpm- G force: 67.2 g and 1500 rpm-G force: 151.2 g, with the rotating tube operating at room temperature. Concentration of the drug 3mg/ml in benzyl alcohol was maintained throughout the experiments.

Table -1: Preparation Meloxicam drug nanoparticles.

Sample No.	Meloxicam		Polymer concentration		Rotation speed (RPM)	Mean particle size & Polydispersity Index(PDI)	Encapsulation Efficiency %
	Con.in Benzyl alcohol (mg/mL)	Flow rate (ml/sec)	Con. in aqueous solution (%wt/v)	Flow rate (mL/sec)			
1	3	0.3	0	0.6	500	156(∂±30) 0.123±0.001	-
2	3	0.3	0	0.6	1000	50(∂±23) 0.092±0.001	-
3	3	0.3	0	0.6	1500	30(∂±10) 0.098±0.001	-
4	3	0.3	0.15	0.6	1000	30(∂±15) 0.134±0.001	57.6
5	3	0.3	1	0.6	1000	116(∂±10) 0.164±0.001	95.4
6	3	0.3	2	0.6	1000	180(∂±18) 0.223±0.001	97.6

Surfactant concentrations were varied (0% to 2 wt %/v) along in establishing the optimal conditions. The nanoparticles were spontaneously formed along the rotating platform by the addition of the drug dissolved benzyl alcohol to polymer dissolved aqueous solution. The nanosuspensions formed at various polymer concentrations and rotation speeds (Table-1) were stored in glass bottles. To evaluate the redispersibility and to study the physio chemical properties of the nanosuspensions, they were freeze-dried (Labconco freeze dryer model 75035, Labconco Corporation, Kansas City, MO).

Characterization:

Characterization for bulk measurement of the particles involved Dynamic Light Scattering (DLS), X-ray Diffraction (XRD) and Differential Scanning Calorimetry (DSC). The size, morphology and properties were examined using high resolution Field Emission Scanning

Electron Microscopy (FESEM), Transmission Electron Microscopy (TEM), and Atomic Force mMicroscopy (AFM).

The PXRD patterns were recorded by a Siemens D5000 Xray diffractometer, in the 2θ range of 2–55◦ using a step size of 0.02◦ and a time step of 5 s with Cu K radiation.

DSC analysis (NETZSCH STA) were carried out on freeze dried samples. Heating rates of 2°C/min, for the temperature range 20 to 300°C were employed. For each experiment approximately 6 mg samples was used.

Surface topography of samples was measured using a Zeiss 1555 Field Emission Scanning Electron Microscopy (FESEM). An emission of 3-5 kV and a working distance of 3-5 mm were used. SEM samples were prepared by applying one drop of nanosuspension on to a metallic sample plate followed by drying, and metalized with platinum.

Transmission Electron Microscopy (TEM) was used to study the morphology, crystallinity of the particles. Measurements were performed using TEM 3000. A drop of nanosuspension were deposited onto the carbon coated TEM and dried by freeze drying (K750X) method.

Atomic Force Microscope (AFM) measurements were made on AFM D5000. AFM samples were prepared by washing the lactose with distilled water, followed by deposition of 10 µl of the colloidal suspension onto freshly cleaved mica plates, dried over 24 h at 25^{o}C.

To determine the drug release from the nanoparticles, 5 mg were added to a beaker containing the dissolution medium (0.1 M pH 7.4 phosphate buffer, 500ml, 25^{o}C,). The dissolution medium was slowly agitated with a magnetic stirrer (Lab-line Multi-magnestir, Lab-Line Instruments, Inc.,Melrose Park, IL). The samples (3 ml) were withdrawn, not replaced, immediately filtered through a 0.01 µm filter (nitrocellulose, Sartorius Filters, Inc., Hayward, CA), and assayed spectrophotometrically (meloxicam, I = 362 nm).

The average particle size and polydispersity of the nanoparticles were determined by Dyanamic light scattering. The mean size of the drug nanoparticles varied from 20 to 200 nm, depending on the process parameters used during the manufacture of the particles. (Fig.1)

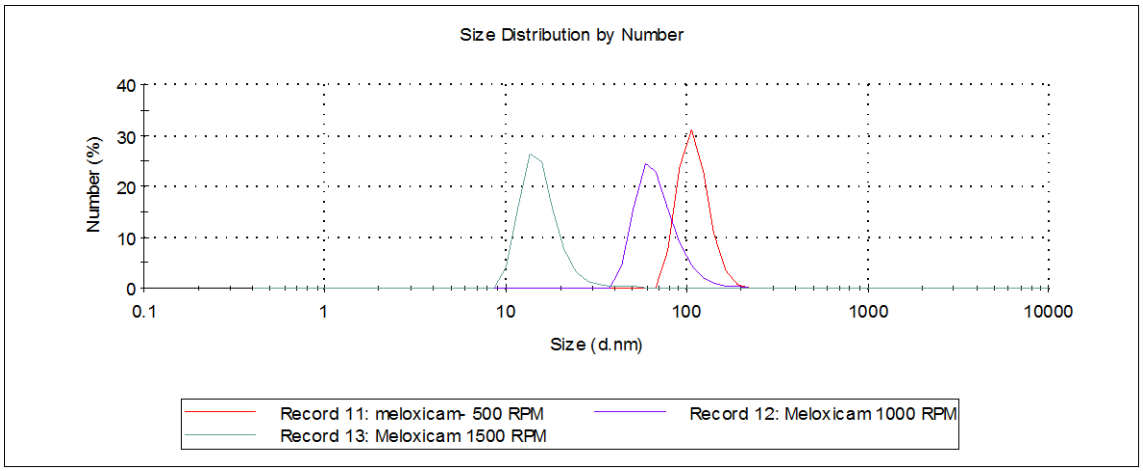

Fig.S1.Particle size distribution curves for meloxicam drug nanoparticles with different rotational speed (No polymer)

Successful formation and surface morphology of the meloxicam-loaded poloxamer 188 encapsulated nanoparticles with 2% wt poloxamer are illustrated by FESEM and AFM phase contrast images in Fig.2.The polymer–drug particles were generally spherical with smooth surfaces.

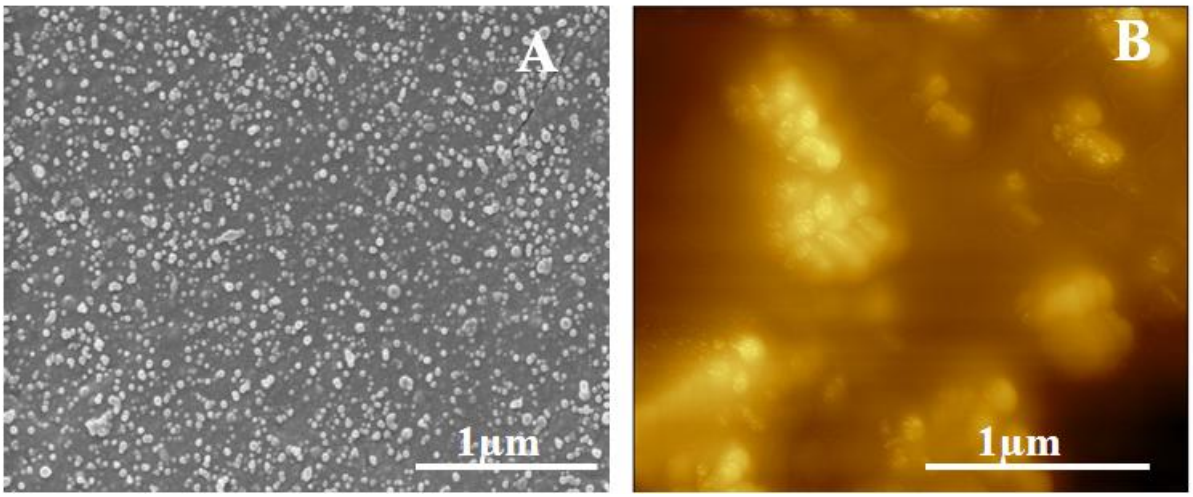

Fig. S2 (A) SEM (B) AFM –images of 2%wt/v Poloxamer encapsulated drug nanoparticles.

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