

Supporting information (ES-1)

L-tyrosine loaded nanoparticles: An efficient catalyst for synthesis of dicoumarols and Hantzsch 1,4-dihydropyridines.

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Materials

L-Tyrosine and Lutrol[®] F-68 (Poloxamer 188) were obtained from Sigma, Mumbai. Eudragit[®] RS100 (Evonik Industries AG, Germany) was obtained from Sandoz Ltd. Mumbai. Distilled- deionized water was prepared with Milli-Q plus System (Elix 10, Millipore corp. India). All other chemicals used were of the highest available grade.

Preparation of LTNPs

LTNPs were prepared with polymer eudragit[®] RS100 using the solvent evaporation (single emulsion) technique with slight modification [Jana et al.¹](#) In brief, the polymeric solution was prepared by adding 100 mg of eudragit[®] RS100 in the mixture of methanol and acetone (20:80 v/v) at room temperature. Weighed quantity of L-tyrosine (equivalent to 10% w/w dry weight of polymer) was dissolved in 1(N) HCl and added to the polymeric solution. The resultant solution was poured into 25 ml of aqueous phase containing 1% (w/v) of poloxamer-188 with a constant flow rate of 1 ml/min. The mixture was then homogenized using a probe homogenizer (VIRTIS, Cyclone IQ, USA), at constant agitation speeds of 10,000 rpm in an ice bath. The formed emulsion was kept at room temperature under gentle stirring for 24 h to evaporate the organic solvents. The prepared polymeric nanoparticle was centrifuged at 18,000 rpm, for 15 min (Sorvall Ultracentrifuge, USA). The nanoparticle was recovered and freeze dried for 2 days (-80 °C and <10 mm mercury pressure, Freezone 6lt, Labconco Corp., MO) to get powdered nanoparticles and stored in freeze.

Characterization of nanoparticles:**Determination of particle size**

Particle size analysis was performed by Photon Correlation Spectroscopy (PCS) with Zetasizer 3000 (Malvern Instruments). The freeze dried powdered samples were suspended in Milli-Q water (1mg/ml) at 25 °C and sonicated for 30 sec in an ice bath before measurement to prevent clumping. The mean particle diameter and size distribution of the suspension were assessed. Analysis was carried out for three times for each batch of sample under identical conditions and mean values were reported.

Atomic force microscopy (AFM)

The surface morphology of prepared nanoparticles was carried out using atomic force microscopy (AFM). The nanoparticle suspension was prepared with milliQ water and dried overnight in air on a clean glass surface and observation was performed with AFM consisting of silicon probes with pyramidal cantilever having force constant of 0.2 N/m. To avoid damage of the sample surface, the tip to sample distance was kept constant. The scan speed of 2 Hz and 312 kHz resonant frequency was used for displaying amplitude, signal of the cantilever in the trace direction and to obtained images.

Transmission electron microscopy (TEM)

Morphology of the particles was also examined using transmission electron microscope. A sample of particle suspension was diluted with 3% w/v phosphotungstic acid adjusted to pH 7.5 with potassium hydroxide corresponding to a 1:1 ratio before examination. One drop of sample was placed for 1 minute on a copper grid coated with a formvar carbon film. The excess of sample was wicked away with the aid of filter paper. The sample was then ready for analysis by TEM.

General procedure for the synthesis of dicoumarols using LTNPs as catalyst (3a-3j)

A mixture of 4-hydroxycoumarin (2 mmol), aldehyde (1 mmol), L-tyrosine loaded nano catalyst (0.02 g), and water (5 ml) was taken in a round bottomed flask and heated on a water bath at 70

°C for specified time (Table 3). The progress of the reaction was monitored by thin-layer chromatography (TLC). Upon completion of the reaction, the mixture was cooled to room temperature. The crude product was extracted with dichloromethane and the catalyst is separated by simple filtration. The dichloromethane extract dried over anhydrous Na_2SO_4 and concentrated to furnish the product.

Synthesis of 1,4-dihydropyridines catalyzed by LTNPs (5a-5o)

In a typical reaction, the aldehyde (1 mmol), methyl/ethyl-acetoacetate (2 mmol), ammonium acetate (1 mmol) and LTNPs catalyst (0.02 g) were stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture is treated with chloroform. The catalyst is separated by simple filtration. The obtained chloroform reaction mixture was concentrated and we got the pure product.

Reference

1. U. Jana, A. K. Mohanty, P. K. Manna and G. P. Mohanta, *Colloids and Surfaces B: Biointerfaces*, 2014, **113**, 269.