

Supplementary Information

**Biodegradable Poly(ϵ -caprolactone) as a Controlled Drug Delivery Vehicle of
Vancomycin for the Treatment of MRSA Infection**

Alok Rai,¹ Sudipta Senapati,² S. K. Saraf,¹ and Pralay Maiti ^{*2}

¹Department of Orthopedics, Institute of Medical Sciences, Banaras Hindu University, Varanasi
221 005, India

²School of Materials Science and Technology, Indian Institute of Technology (Banaras Hindu
University), Varanasi 221 005, India

Drug Release Kinetics

Various kinetic models were used to fit the in vitro PCL-VMC release profiles. The mathematical forms of these models are given below:

(1) The zero-order model describes refers to the process of constant drug release from a drug delivery device and can be represented as

$$M_0 - M_t = k_0 t$$

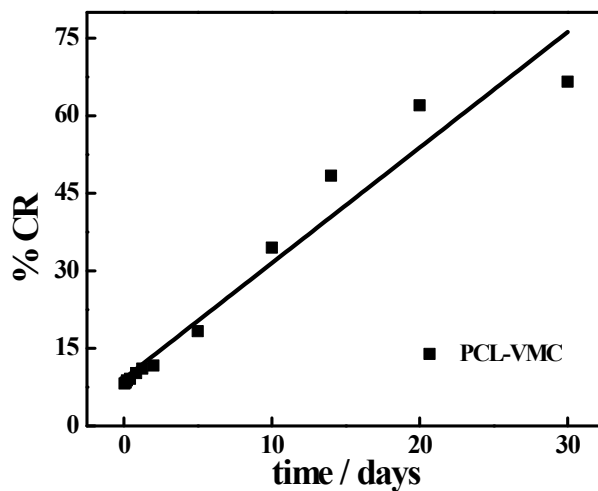


Figure S1: Plot of zero-order kinetic model for PCL-VMC system which gives poor r^2 value (0.93) and is not found suitable to explain the release kinetics.

(2) The first-order model describes the release from systems where dissolution rate depends on amount of the drug (RH) present in the LDH hybrids and can be generally expressed as

$$\log (M_t/M_0) = -k_1 t$$

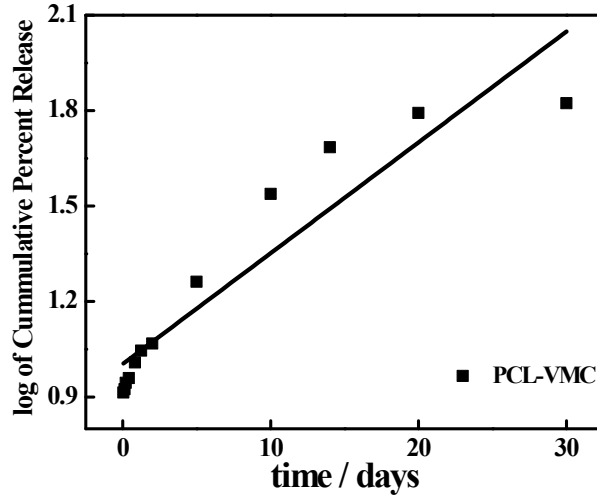


Figure S2: Plot of first-order kinetic model for PCL-VMC system which also gives poor r^2 value (0.87) and is not found suitable to explain the release kinetics.

(3) Higuchi model is based on the hypotheses that (i) initial drug concentration in the hybrid is much higher than drug solubility; (ii) drug diffusion occurs only in one dimension; (iii) thickness of the drug particles are much smaller than that of system; (iv) matrix swelling and dissolution are negligible; and (v) drug diffusivity is constant; and can be generally expressed as

$$f_t = Q = A \sqrt{D(2C - C_s)C_s t}$$

where in time t , Q amount of drug is released from per unit area A , C is the drug initial concentration, C_s is the drug solubility in the hybrid media and D is the diffusion coefficient of the drug molecules in the matrix substance.

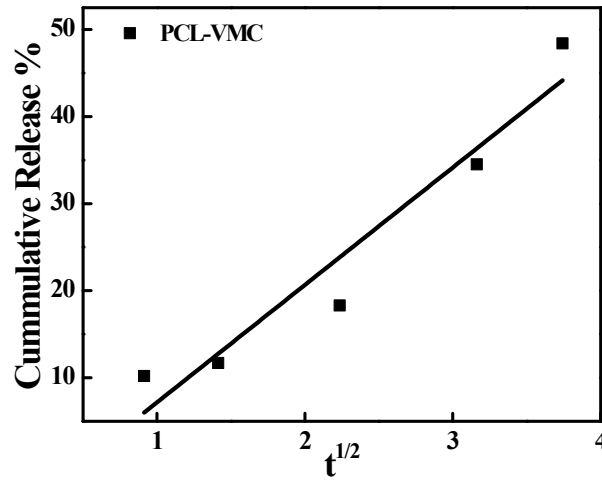


Figure S3: Plot of Higuchi kinetic model for PCL-VMC system which gives poor r^2 value (0.924) and is not found suitable to explain the release kinetics.

(4) To investigate the kinetics of drug release, first 60% drug release data were fitted in Korsmeyer-Peppas models and can be represented as

$$M_t/M_\infty = Kt^n$$

where M_t / M_∞ is a fraction of drug released at time t , k is the release rate constant and n is the release exponent.

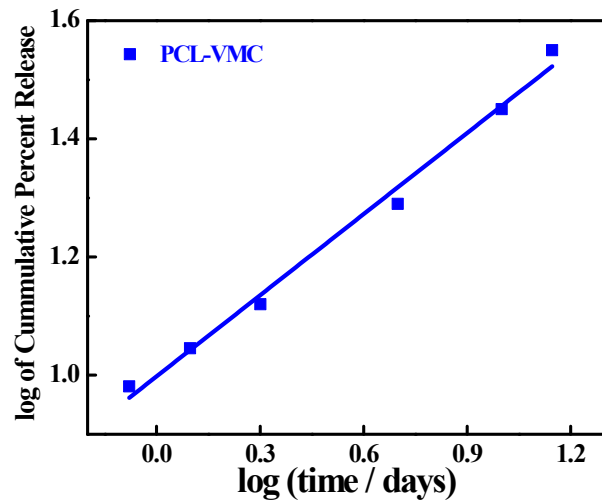


Figure S4: Plot of Korsmeyer-Peppas models for PCL-VMC system which explains the release kinetics more reasonably (r^2 value 0.991).

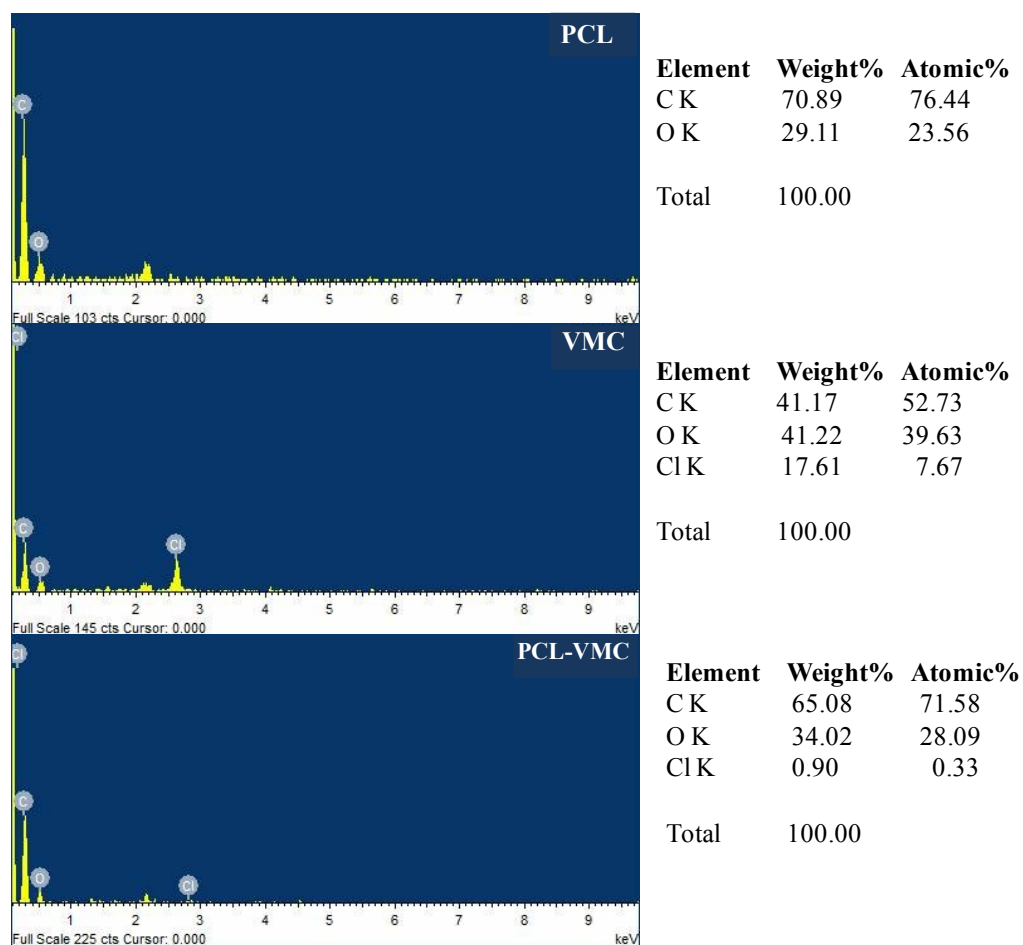


Figure S5: Energy-dispersive X-ray spectroscopy (EDAX) patterns showing elements present in pure PCL, VMC and PCL–VMC hybrid. The predominant components were found to be carbon (C) and oxygen (O) for pure PCL; carbon (C), oxygen (O) and Chlorine (Cl) for VMC and carbon (C), oxygen (O) and Chlorine (Cl) for PCL–VMC hybrid.



Figure S6: Clinical examination of the operative site for the PBS treated group showing gradual increase of infection (white pus) with time.



Figure S7: Post-operative radiographs of PBS treated group rabbit limbs at 10, 30 and 45 days.

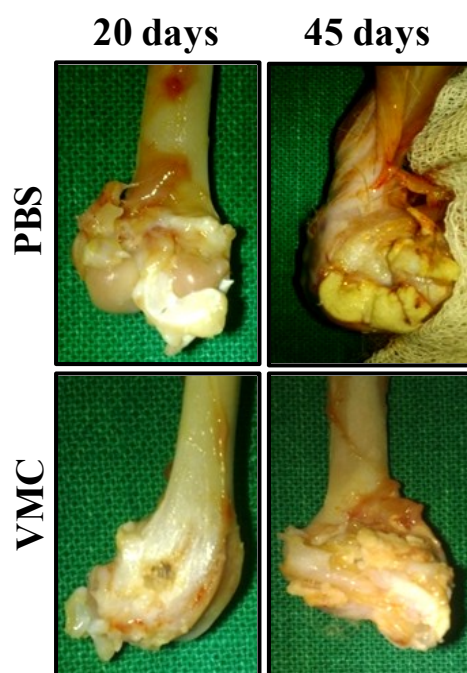


Figure S8: Gross examination of rabbit limbs at 20 and 45 post operative days for PBS and pure VMC treated groups.

Table S1: Mean bacterial count of MRSA strain in various groups.

Time / days	Control	PCL-VMC
5	3.4×10^6 CFU/gm	$2. \times 10^4$ CFU/gm
10	2.8×10^6 CFU/gm	0 CFU/gm
15	2.6×10^6 CFU/gm	0 CFU/gm