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Phosphorylated Chitosan Armed Hydroxyapatite Nanocomposite for Advancing Activity on *Osteoblast* and *Osteosarcoma* cells

Murugan Sumathra[a], Mariappan Rajan[a]*, Murugan A Munusamy[b]

[a*] Biomaterials in Medicinal Chemistry Laboratory, Department of Natural Products Chemistry, School of Chemistry, Madurai Kamaraj University, Madurai 625021, Tamil Nadu, India.

[b]Department of Botany and Microbiology, College of Science, King Saud University, Riyadh, Saudi Arabia

*Corresponding authors:

Mariappan Rajan - Tel: +91 9488014084; Fax: 0452-2459845; Email: rajanm153@gmail.com

S1. *Invitro* studies

As shown in Figure S1(A), the drug encapsulation efficiency for HAP/PCS reached approximately 85.3%, which is satisfactory for a drug delivery system. After 4 days, the release was increased and the 6-gingerol concentration in the medium changed after 20 days. In addition, the amount of 6-gingerol released from the composite was significantly higher. The results revealed that 94.80% of 6-gingerol was released from the loaded HAP/PCS composite after 20 days. The UV release profile is presented in Figure S1(B).

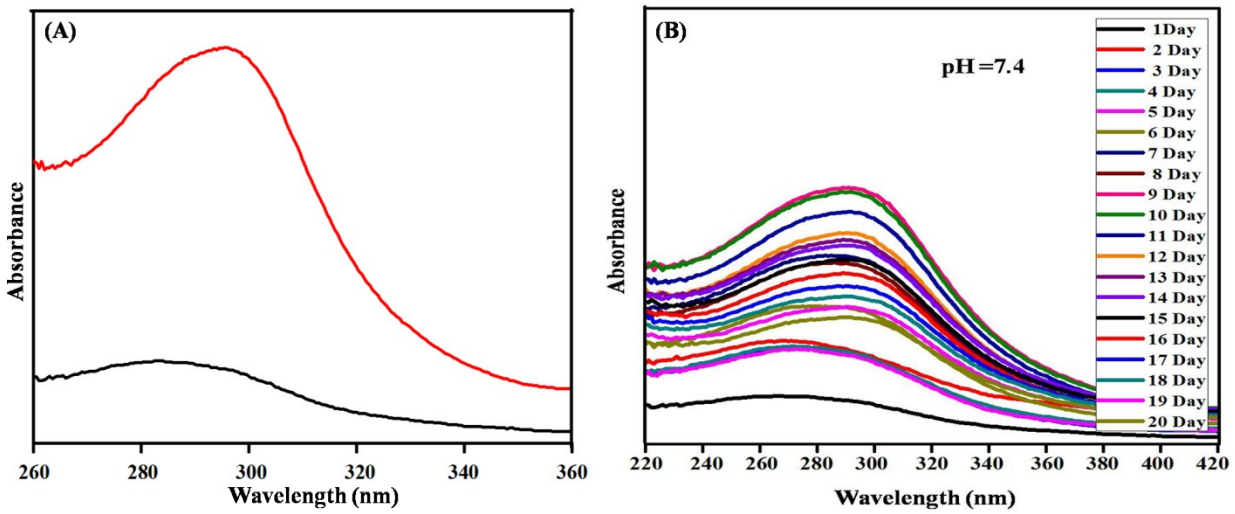

Figure S1.(A)Encapsulation efficiency of 6-gingerol on PCS-HAP;(B) UV spectra for *Invitro* drug release of 6- gingerol from HAP/PCS/G in PBS at pH 7.4

S2.Water uptake, Porosity, Degradation studies

The water uptake of the material affects the release of the loaded sample by diffusion and the rate of degradation of the material [53]. The percentage difference in weights before and after water uptake was recorded. As shown in Figure 2(A & B), a significant increase in water uptake and degradation was observed after addition of the PCS moiety. The more crystalline chitosan might act as an absorption barrier and limit the amount of water penetrating the composite

structure, despite its hydrophilicity [54]. The results of water uptake analysis showed a strong correlation with the porosities of samples, as both have a direct relationship with PCS.

The results of porosity analysis indicated that by the addition of PCS, the probable mechanism underlying particle formation could be elucidated. Although the combined effect of external energy and temperature inside the particles was modulated, the porosity was maintained on the surface as well as inside the particles. Here, the porosity was enhanced by sonication of the HAP/PCS/G composite, and porosity up to 80% was attained (Fig. S2(B))compared with the previous report on HAP cements and commercially available HA cements, which showed a dispersion of 40% and attained a porosity of up to 70%.

The results indicated that scaffold biodegradability increased after the introduction of PCS. A desired tissue engineering scaffold must meet specific biodegradability requirements. The incorporation of 0.5% PCS yields acceptable results. The requirement for a specific tissue engineering application can be satisfied by adding PCS. The application of ultra-probe sonicated and lyophilized PCS resulted in increased degradation properties, possibly due to the binding of HAP/PCS after implantation, as shown in Figure S2(C).

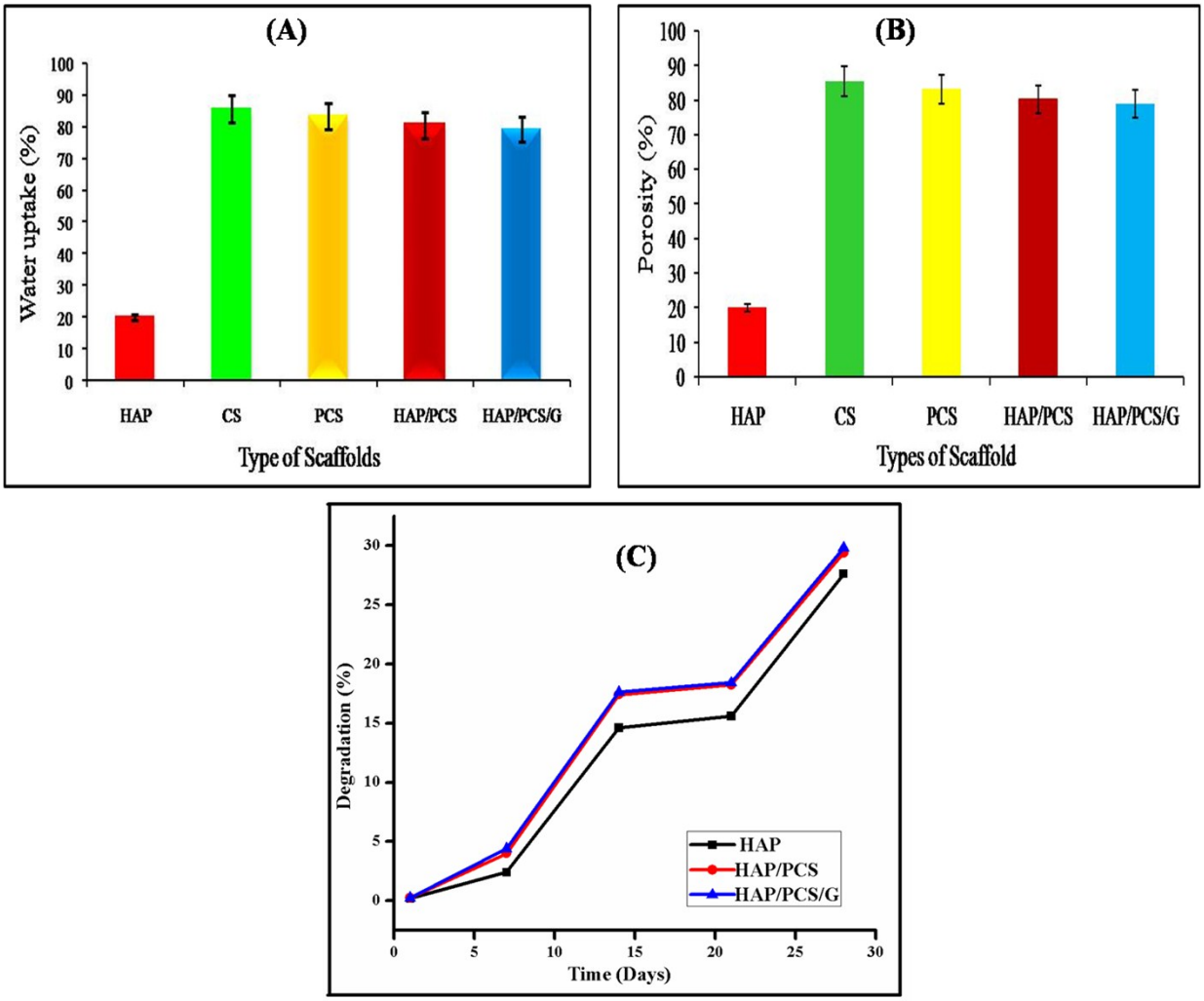

Figure S2. (A)Water uptake studies (B) Porosity studies (C) Biodegradation studies

S3. BET and BJH Analysis

Table.S1 Average Surface and structural parameters of HAP/PCS nanocomposite

Surface Area (m^2/g)	Pore Volume (Cm^3/g)	Pore diameter(nm)
4.1	6.25	5.5