

Data Interpretation Paradoxes in a Nanoencapsulated α -Mangostin Hydrogel Film for Anti-Acne Therapy [Letter]

Zhenzhen Xiao¹, Yingjian Tan² 

¹Department of Dermatology, Fuzhou First General Hospital, Fuzhou, People's Republic of China; ²Department of Dermatology, Venereology and Allergology, Charité-Universitätsmedizin Berlin, Berlin, 10117, Germany

Correspondence: Yingjian Tan, Email Dr.yingjian.tan@gmail.com

Dear editor

We read with great interest the article by Yuniarsih et al on nanoencapsulated α -mangostin loaded chitosan-alginate hydrogel films for topical anti-acne therapy.¹ The authors are commended for addressing the urgent need for antibiotic-free alternatives in acne management, and the development of a biocompatible film formulation is conceptually appealing. However, we have identified three critical methodological inconsistencies that fundamentally challenge the validity of the reported conclusions. These issues relate to invalid bacterial enumeration, misinterpretation of nanoparticle size distribution, and a charge-state contradiction that negates the claimed core-shell structure.

First, the methodology clearly states that only plates with colony counts ranging from 30 to 300 are considered valid for enumeration; plates with total colonies fewer than 30 are deemed to contain excessively low bacterial loads and yield invalid data. However, Table 5 shows that the viable bacterial load of the core experimental group (HF α -M NPs) is (2.46×10^1) CFU/g (24.6 CFU/g), while the positive control clindamycin gel group yields (2.21×10^1) CFU/g (22.1 CFU/g). Both values fall below the 30-colony threshold and fail to meet the criteria for valid counting. Nevertheless, the authors draw conclusions that the nanoencapsulated hydrogel film exhibits superior antibacterial activity with efficacy comparable to clindamycin based on these invalid datasets. The quantitative antibacterial assay suffers from fundamental flaws, and the *in vivo* anti-inflammatory and tissue repair benefits claimed by the authors lack robust experimental evidence.

Second, the authors misinterpret a polydispersity index (PDI) of 0.450 as indicating a “relatively homogeneous size distribution, supporting formulation stability”. In dynamic light scattering (DLS) principles, a PDI >0.3 signifies a highly polydisperse size distribution, indicating a propensity for aggregation, Ostwald ripening, and unpredictable release kinetics.^{2,3} Polydisperse systems inherently lack batch-to-batch reproducibility and uniform drug release, directly contradicting the authors' claims.

Third, the reported zeta potential contradicts the claimed core-shell structure. The nanoparticles were designed as a chitosan core coated with anionic sodium alginate. However, the reported zeta potential is +40.9 mV. Because alginate is a strongly negatively charged polyanion, a successful coating would reverse the surface charge to a negative value or bring it near neutral, depending on the deposition layers.⁴ The highly positive +40.9 mV charge exposes an uncoated, bare chitosan surface, proving the alginate coating failed or is entirely absent. This negates the intended controlled-release carrier function, as the system is functionally just an uncoated chitosan particle.

In summary, we appreciate the translational ambition of this work, but the bacterial enumeration violates the authors' own quantitation rules, the PDI misclassification misrepresents formulation quality, and the zeta potential exposes a failed coating strategy. These are not mere minor clarifications—they strike at the core of the efficacy claims and the proposed mechanism of action. We urge the authors to provide raw data, re-evaluate their enumeration methods, and confirm the actual coating status before asserting therapeutic superiority. Clarification of these points would substantially strengthen the scientific basis of the study.

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