Free Drug vs. Nanomedicine in Transdermal Patches: A Comparative Exploration of Etoricoxib Drug Release and Its Analgesic Activity

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Abstract. Transdermal patches of traditional Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as diclofenac are already commercially available. Both diclofenac and etoricoxib (EB) are members of the NSAID family and are used as pain and inflammation relievers. However, transdermal formulations of EB, a non-traditional NSAID, have not yet been developed. The primary cause for the lack of such formulation might be the very poor aqueous solubility of EB. The traditional NSAIDs (non-selective COX inhibitor) raises the risk of renal damage, cardiovascular events and gastrointestinal side effects. EB is a selective COX-2 inhibitor and may have a lower risk of causing harm compared to traditional NSAIDs. Therefore, the transdermal patches of EB must be made highly desirable for patients requiring long-term pain management. This study presents the development of EB nanomedicine-impregnated transdermal patches to overcome its poor aqueous solubility and improve its therapeutic efficacy. The nanomedicines of EB were produced by encapsulating the drug into silica nanoparticles (SNPs) and sodium montmorillonite (Na-MMT) nanoclay, leveraging their high surface area, biocompatibility and ability to enhance solubility and skin permeation. The transdermal patches were fabricated incorporating the pure drug as well as nanomedicines to execute a comparative analysis between the patches with and without nanocarriers, performing various pharmaceutical experiments such as *in vitro* drug release study at pH 5.5 and 7.4, skin irritation study on mice and rats, *ex vivo* skin permeation study using Franz diffusion cell, *ex vivo* drug release kinetics analysis and *in vivo* analgesic activity via Hot-Plate and Tail-Flick methods.

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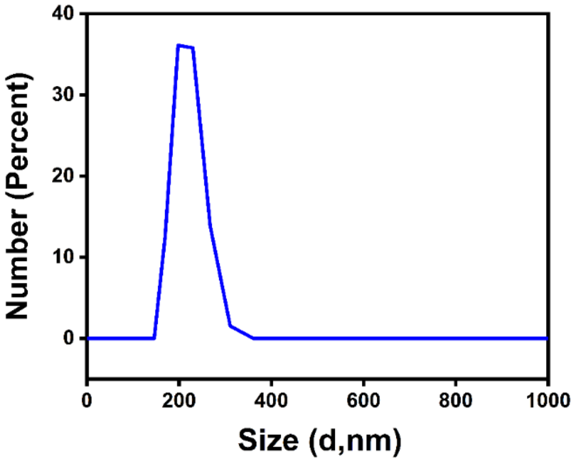

Fig SP1. Particle size distribution curve of acid-catalyzed SNPs, P1 (Source: Ref. Sourav Adhikary et al. Appl. Biochem. Biotechnol., 2023, 195, 4712-4727. Reproduced with permission from © 2023, Springer Nature)

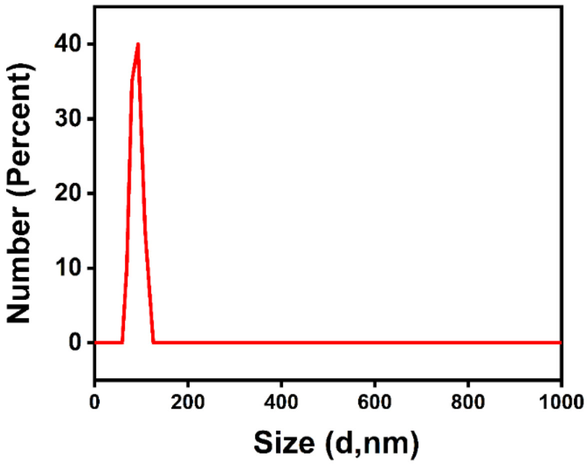

Fig SP2. Particle size distribution curve of base-catalyzed SNPs, P2 (Source: Ref. Sourav Adhikary et al. Appl. Biochem. Biotechnol., 2023, 195, 4712-4727. Reproduced with permission from © 2023, Springer Nature)

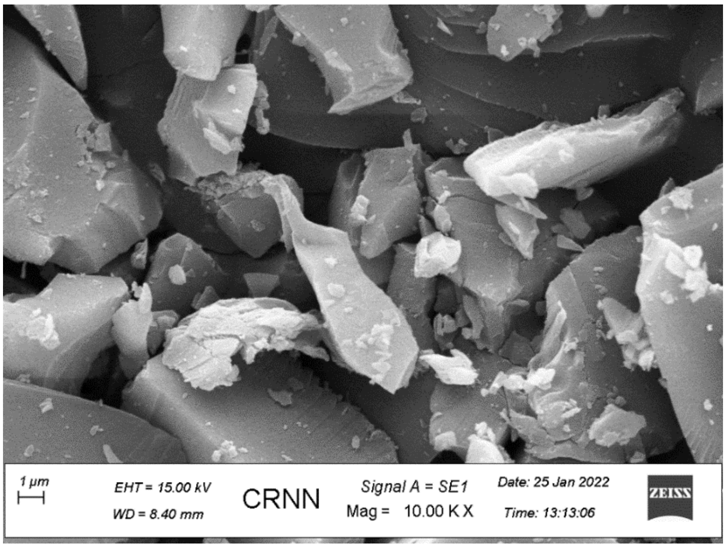

Fig SP3. SEM image of acid-catalyzed SNPs, P1 showing irregular morphology of the particles (Source: Ref. Sourav Adhikary et al. Appl. Biochem. Biotechnol., 2023, 195, 4712-4727. Reproduced with permission from © 2023, Springer Nature)

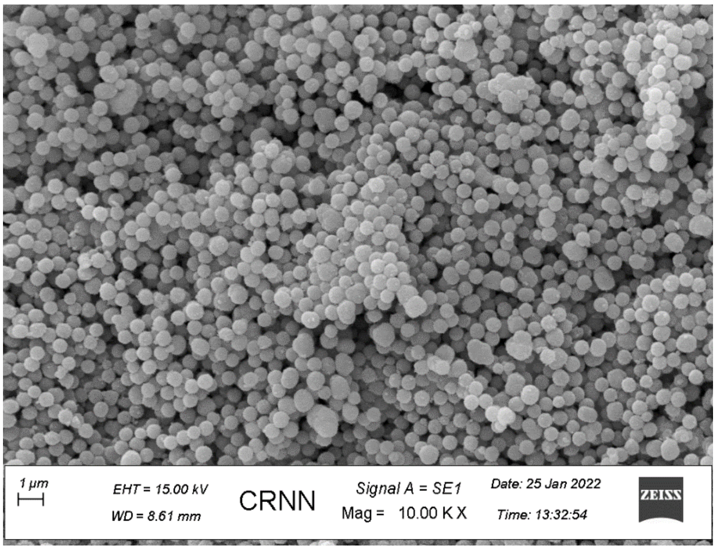

Fig SP4. SEM image of base-catalyzed SNPs, P2 showing spherical morphology of the particles (Source: Ref. Sourav Adhikary et al. Appl. Biochem. Biotechnol., 2023, 195, 4712-4727. Reproduced with permission from © 2023, Springer Nature)

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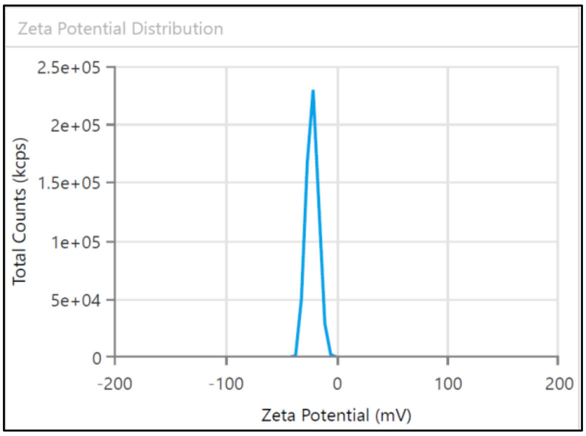

Fig SP5. Zeta potential distribution curve of acid-catalyzed SNPs, P1

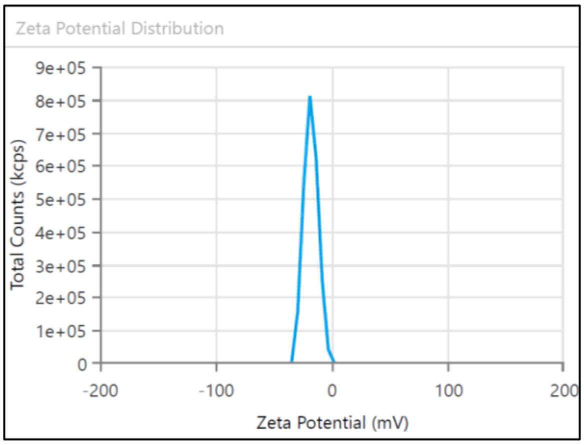

Fig SP6. Zeta potential distribution curve of base-catalyzed SNPs,