Nanovesicular formulations of estrogenic soft drugs as components of nanohybrid hydrogel for advanced wound care

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Estrogens are steroid hormones with well-documented roles in wound healing, but their systemic administration causes significant side effects. To overcome this drawback, active molecules can be converted into Soft Drugs, thus confining their action to the application site. In a previous study, two estrogenic soft drugs with a hydrolysable ester group, **1** and **2** , were identified as the most promising candidates for topical application [1,2] .
In this work, compounds **1** and **2** were formulated in nanovesicular carriers, namely liposomes and transfersomes, and then loaded in hydrogel in order to obtain hybrid nanosystems, potential suitable for direct topical application (*Figure 1*). Nanovescicular formulations [3] were prepared using a phosphocholine (dipalmitoylphosphatidylcholine, DPPC, or dimyristoylphosphatidylcholine, DMPC) as the main component, in mixture with the estrogen derivative (**1** or **2**) and/or sodium cholate as edge activator. Formultions were physicochemically characterized by DLS and DELS analysis. The entrapment efficiency of **1** and **2** was assed by UV-Vis measurements. In addition, the leakage of estrogenic compounds was monitored over 24h.
Finally, the nanovesicular systems were adsorbed into gel matrices properly selected for their ability to maintain moisture, mimic the extracellular matrix, and support tissue regeneration, with the final goal to obtain suitable wound dressing. To this aim, a protein-polysaccharide hydrogel blend based on gelatin type A (GEL) and gellan gum (GG), respectively, was firstly developed. Afterwards, an interconnected porous membrane was prepared by a controlled freeze-drying process. Neat and loaded GEL/GG dressings were characterized in terms of morphological, physicochemical and biological properties by using human dermal fibroblasts.

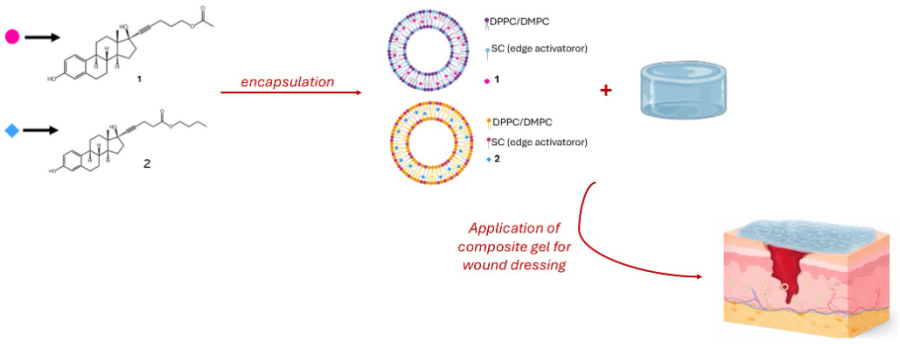

Figure 1: Transdermal nanocomposite drug delivery systems

References:

[1] Brufani et al., Molecular Pharmaceutics, **2009** , 6 (2), 543-556.
[2] Brufani et al., Scientific Reports, **2017** , 7: 2510.
[3] Hua S., Lipid-based nano-delivery systems for skin delivery of drugs and bioactives, Frontiers in Pharmacology, **2015** , **6** , 219.