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Design and Evaluation of Nanocarrier Embedded Hybrid Hydrogels for Topical Delivery of Hydrophobic Molecules

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Extended Abstract

Menopause is a substantial event in women's life as it significantly impacts their physiological and psychological wellbeing. As menopause commences, oestrogen and progesterone hormone productions are greatly reduced due to ovarian follicle depletion, resulting diverse symptoms e.g. vasomotor symptoms (hot flashes, osteoporosis), psychological symptoms (anxiousness, depression, excitation, irritability, mood swings), and physical symptoms (fatigue, insomnia, vertigo, tachycardia, weight gain, muscle & joint ache, breathing problem, vaginal dryness, bladder control problem) [1, 2]. Despite 2- to 4-folds higher chance of having clinical symptoms [3], which reduces quality of life in many women [4], hormone-replacement therapy (HRT) for postmenopausal women are often neglected, especially in developing countries like Bangladesh. Until now, no HRT formulations are produced locally or imported despite having over 80 million women population and well-established local pharmaceutical companies (which exports medicines to many European countries).

The typical HRT in menopause is oestradiol (E2). There are many E2 formulations available worldwide for HRT, chiefly as hydrogels or as transdermal patches. The hydrogels formulations are generally applied daily, whereas the patches are replaced every 3-4 days. Even Though patches can provide sustained release of E2, the inconvenience of carrying an external sticky material on the skin reduces its patient compliance. Moreover, patches are more expensive compared to hydrogels making it less accessible for developing countries. The aim of this project is to design lipid core nanocarriers (LCN) embedded hydrogels (HLCN) to provide sustained transdermal delivery of E2 to improve patient compliance, and to reduce treatment cost compared to transdermal patches. The LCNs can release hydrophobic drugs in a sustained manner [5] and can be used for transdermal delivery of hydrophobic drugs [6].

Several LCN-E2 formulations were prepared using phase-inversion technique. The formulations were evaluated for their particle size, percentage E2 encapsulation, and percent drug loading. The results were analysed to understand the effects of various LCN ingredients on E2 entrapment and %w/w drug loading. Afterwards, carbomer hydrogel systems (HLCN-E2) which entraps LCN-E2 in its matrix were prepared. The HLCN-E2s were evaluated for their %w/w E2-loading, pH and spreadability. The results were compared with commercial topical hydrogel preparations. The experiments on drug release, stability and *in vitro* transmembrane permeability are ongoing.

The particle size of the LCNs were found between 23-95 nm. The percent drug loading and encapsulation efficiency of LCN-E2 were observed to increase with increasing ratio of the surfactant on LCN surface. The % drug loading of HLCN-E2 were much higher (without the use of alcohol or any other organic solvents), compared to commercial E2 hydrogels. The pH of the HLCN-E2 reduced gradually from 6.4 to 6.2 as polymer concentration increased progressively from 2.0 to 3.0 %. The spreadability of the formulations were comparable to the commercially marketed hydrogels.

The initial findings of other study showed were encouraging. Further studies are necessary to optimize the formulation and further enhance its delivery efficiency. Properly formulated hybrid hydrogel systems have the potential to fill up the market gap between immediate release hydrogels and sustained release patches.

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