World Academy of Science, Engineering and Technology
International Journal of Health and Medical Engineering
Vol:17, No:06, 2023

Baricitinib Lipid-based Nanosystems as a Topical Alternative for Atopic Dermatitis Treatment

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Abstract : Atopic dermatitis (AD) is a persistent skin condition characterized by chronic inflammation caused by an autoimmune response. It is a prevalent clinical issue that requires continual treatment to enhance the patient's quality of life. Systemic therapy often involves the use of glucocorticoids or immunosuppressants to manage symptoms. Our objective was to create and assess topical liposomal formulations containing Baricitinib (BNB), a reversible inhibitor of Janus-associated kinase (JAK), which is involved in various immune responses. These formulations were intended to address flare-ups and improve treatment outcomes for AD. We created three distinct liposomal formulations by combining different amounts of 1-palmitoyl-2-oleoyl-glycero-3-phosphocholine (POPC), cholesterol (CHOL), and ceramide (CER): (i) pure POPC, (ii) POPC mixed with CHOL (at a ratio of 8:2, mol/mol), and (iii) POPC mixed with CHOL and CER (at a ratio of 3.6:2.4:4.0 mol/mol/mol). We conducted various tests to determine the formulations' skin tolerance, irritancy capacity, and their ability to cause erythema and edema on altered skin. We also assessed the transepidermal water loss (TEWL) and skin hydration of rabbits to evaluate the efficacy of the formulations. Histological analysis, the HET-CAM test, and the modified Draize test were all used in the evaluation process. The histological analysis revealed that liposome POPC and POPC:CHOL avoided any damage to the tissues structures. The HET-CAM test showed no irritation effect caused by any of the three liposomes, and the modified Draize test showed a good Draize score for erythema and edema. Liposome POPC effectively counteracted the impact of xylol on the skin, and no erythema or edema was observed during the study. TEWL values were constant for all the liposomes with similar values to the negative control (within the range 8 - 15 g/h·m2, which means a healthy value for rabbits), whereas the positive control showed a significant increase. The skin hydration values were constant and followed the trend of the negative control, while the positive control showed a steady increase during the tolerance study. In conclusion, the developed formulations containing BNB exhibited no harmful or irritating effects, they did not demonstrate any irritant potential in the HET-CAM test and liposomes POPC and POPC:CHOL did not cause any structural alteration according to the histological analysis. These positive findings suggest that additional research is necessary to evaluate the efficacy of these liposomal formulations in animal models of the disease, including mutant animals. Furthermore, before proceeding to clinical trials, biochemical investigations should be conducted to better understand the mechanisms of action involved in these formulations.

Keywords : baricitinib, HET-CAM test, histological study, JAK inhibitor, liposomes, modified draize test
Conference Title : ICSDISC 2023 : International Conference on Skin Disorders, Infections and Skin Care
Conference Location : London, United Kingdom
Conference Dates : June 22-23, 2023