molecular pharmaceutics

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Colloidal Vesicular System of Inositol Hexaphosphate to Counteract DMBA Induced Dysregulation of Markers Pertaining to Cellular Proliferation/Differentiation and Inflammation of Epidermal Layer in Mouse Model

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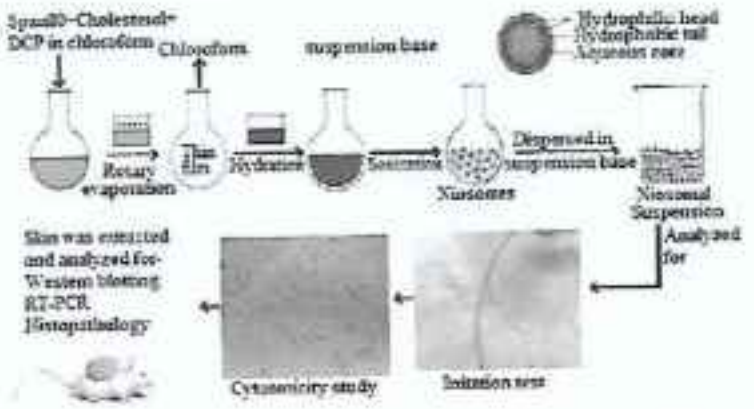
Supporting Information

ABSTRACT: Cancer is a global health problem and chemoprevention is a promising approach for reducing cancer burden. Inositol hexaphosphate (IP6), a natural bioactive constituent of cereals, legumes, etc., has momentous potential as an antiangiogenic agent, that specifically affects malignant cells. The shortcoming is its quick absorption on oral/topical administration. Niosomes are flexible carriers for topical drug delivery. The central venture of current research was to optimize and characterize niosomal delivery system of IP6 for treatment of skin cancer. Thin film hydration method was utilized to prepare IP6 niosomes, and these were dispersed as a suspension in a suitable base. Developed formulations were analyzed for various physicochemical and pharmacological parameters such as particle size, encapsulation efficiency, morphology, drug release, texture analysis, irritability, cell line studies, Western blotting, RT-PCR, and histopathology. IP6 niosomal suspension and IP6 in acetone displayed IC_{50} value at the concentration of 0.96 mM (0.63 mg/mL) and 1.39 mM (0.92 mg/mL), respectively. IP6 niosomal suspension showed significantly higher ($p < 0.05$) activity and showed cytotoxic effect in SK-MEL-2 cancer cell line. Crucial events of cellular proliferation and differentiation, like expression of ornithine decarboxylase (ODC), proliferating cell nuclear antigen (PCNA), cycloxygenase-2 (COX-2) and Cyclin D1 were initiated from the fourth hour through application of 7,12-dimethylbenzanthracene (DMBA) on albino mice. The DMBA altered expression of aforesaid enzymes was significantly ($P < 0.001$) prevented by concomitant application of niosomal formulations. Results of cell line study, Western blotting, RT-PCR, and histopathology suggested that IP6 niosomal suspension could constitute a promising approach for prevention of cellular proliferation as well as DMBA induced dysregulation of cellular proliferation/differentiation and inflammation.

KEYWORDS: *skin cancer, phytic acid, niosomes, suspension, SK-MEL-2 cell line, histopathology, Western blotting, RT-PCR*



INTRODUCTION

Cancer remains a life threatening disease, and various efforts to contain the same have hitherto proved almost futile.[1] On an average, 3−8% increase in skin cancer per year has been recorded, with >1 million new cases every year.[2] Globally, people still rely on herbal medicines as first line treatment, owing to their perception of safety and general acceptance for cancer prevention as well as treatment. The wide investigation has identified numerous dietary, botanical, and natural compounds that have chemopreventive properties.[3,4]

Inositol hexaphosphate (IP6), commonly known as phytic acid, is a natural bioactive constituent of grains, legumes, and cereal products.[5,6] Chemically, IP6 is a simple carbohydrate with six phosphates attached to each carbon (inositol-1,2,3,4,5,6-hexaphosphate) and a principal storage of phosphorus in several plant tissues.[7,8] It possesses various health benefits such as lowering of serum cholesterol, strong antioxidant properties, etc. It has also been revealed to have significant potential as an antiangiogenic agent that only affects malignant

Received: December 21, 2016
Revised: February 2, 2017
Accepted: February 7, 2017
Published: February 7, 2017

DOI: 10.1021/acs.molpharmaceut.6b01147
Mol. Pharmaceutics XXXX, XXX, XXX−XXX