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ORIGINAL ARTICLE

Process optimization and photostability of silymarin nanostructured lipid carriers: effect on UV-irradiated rat skin and SK-MEL 2 cell line

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Abstract The objective of the present work was to formulate a novel stable delivery system which would not only overcome the solubility issue of silymarin, but also help to increase the therapeutic value by better permeation, anticancer action and reduced toxicity. This was envisaged through the recent developments in nanotechnology, combined with the activity of the phytoconstituent silymarin. A 2^3 full factorial design based on three independent variables was used for process optimization of nanostructured lipid carriers (NLC). Developed formulations were evaluated on the basis of particle size, morphology, in vitro drug release, photostability and cell line studies. Optimized silymarin-NLC was incorporated into carbopol gel and further assessed for rheological parameters. Stable behaviour in presence of light was proven by photostability testing of formulation. Permeability parameters were significantly higher in NLC as compared to marketed phytosome formulation. The NLC based gel described in this study showed faster onset, and prolonged activity up to 24 h and better action against edema as compared to marketed formulation. In case of anticancer activity of silymarin-NLC against SK-MEL 2 cell lines, silymarin-NLC proved to possess anticancer activity in a dose-dependent manner (10–80 μM) and induced apoptosis at 80 μM in SK-MEL 2 cancer cells. This work documents for the first time that silymarin can be formulated into nanostructured lipoidal carrier system for enhanced permeation, greater stability as well as anticancer activity for skin.

Keywords Lipoidal carrier · Skin cancer · Apoptosis · NLC · Factorial design

Introduction

Nanotechnology promises superior treatment and management of chronic diseases such as cancer. Several advantages, such as low skin irritation, increased protection of encapsulated drug and increased penetrability through the skin are offered [1–3]. Solid lipid nanoparticles (SLN) were developed as an alternative colloidal carrier system to emulsion, liposomes and polymeric nanoparticles [4]. SLNs had the drawback of drug leakage after long-term storage, and drug expulsion due to an ongoing crystallization process of the lipid towards a perfect crystal [1, 2]. Nanostructured lipoidal carriers (NLC) were developed to overcome potential limitations associated with SLNs and are the second generation nanoparticles composed of solid and liquid lipid matrix. NLC composed of diverse oils with solid lipid, can produce imperfections in their lattice structure and create separation in the fatty acid chain packing, making more space for the drug [2, 3]. Liquid lipids are better solubilizers for drugs as compared to solid lipids [9]. Miglyol 812 (a mixture of triglycerides), was selected as the lipid of choice based on composition of the epidermis which is mainly triglycerides (25 %), by virtue of its low viscosity, and because of its ability of lowering prostaglandin E2, which is a pro-inflammatory mediator. Compritol 888 ATO (glyceryl dibehenate) was taken as the solid lipid, which is suitable for production of lipid nanoparticles [10–13]. There are numerous methods to produce lipid nanoparticles such as micro emulsion method, solvent

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