Limonene as a vehicle in topical delivery of carvedilol for skin cancer chemoprevention

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Skin cancer is currently one of the most common cancers and is defined as an abnormal growth of the skin cells. The goal of this study is to develop a topical delivery system of carvedilol with limonene as the vehicle. Limonene is a major component found in the rinds of citrus fruits and other herbs. It is one of many natural compounds that have demonstrated inhibitory activity in different types of cancers such as breast, lung, and stomach cancer. Furthermore, limonene has shown to increase skin permeation of drugs including carvedilol. The soft agar colony formation assay was used to evaluate anchorage-independent growth of JB6 mouse epidermal cells. This assay tested concentrations of carvedilol (0.1, 1.0 and 10 μM); limonene (1.0, 10, 100 and 1000 μM); and a combination of carvedilol (1.0 μM) and limonene (1.0, 10 or 100 μM). Results demonstrated that carvedilol and limonene as single treatment inhibited colony formation. The combination of carvedilol and limonene showed higher colony inhibition than single treatment, although not statistically significant. Franz diffusion cell was used to test for permeation of the drug. The device has two chambers separated by a membrane, which in this case is rat skin. The drugs, in vehicles of 40% polyethylene glycol (PEG) 400 in PBS or 40% PEG400 in PBS plus 5% limonene were applied into the donor chamber while the samples are collected through the receptor chamber as the drug permeates through the skin. The samples were collected at 16 hours, 20 hours, and 24 hours. Results showed that limonene significantly increased permeation. Therefore, our data indicate that limonene was able to increase skin permeation and the chemopreventive activity of carvedilol. This new formulation will be further examined in animal models for its efficacy against UV-induced skin cancer.