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POSTER PRESENTATIONS


Solid lipid nanoparticles of anticancer drug andrographolide: formulation, in vitro and in vivo studies

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Abstract
Diterpenoidal anti-cancer drug andrographolide (AD) was encapsulated into solid lipid nanoparticle (SLN) because of poor aqueous solubility and high lipophilicity. AD-SLNs were prepared by solvent injection method and characterized for droplet size, surface morphology, zeta potential, etc. In vitro drug release was carried out by dialysis-membrane method. A pharmacokinetic study was performed by UPLC/Q-TOF-MS method to determine the maximum plasma concentration (C_max), area under the curve (AUC), etc. There was an improvement in C_max and AUC of AD-SLNs when compared with AD, thereby enhancing the bioavailability of AD. The t_max was increased than that of AD suspension, indicating the sustained release pattern of AD-SLNs. The antitumor activity was carried out on Balb/c mice showing better results with AD-SLNs as compared to AD. Thus, the AD-loaded SLNs would be useful for delivering poorly water-soluble AD with enhanced bioavailability and improved antitumor activity.

Keywords
Andrographolide, antitumor activity, pharmacokinetics, solid lipid nanoparticles, UPLC/Q-TOF-MS method

Introduction
Andrographolide (AD) is a labdane diterpenoid, obtained from the herb Andrographis paniculata and is responsible for most of its pharmacological properties including anti-cancer activity. The compound is able to induce a G0/G1 cell-cycle arrest in various kinds of cancer cell, activates the death receptor pathways, induces TRAIL (TNF-related apoptosis-inducing ligand)-mediated apoptosis and causes inhibition of NF-11B transcriptional factors and various angiogenic factors. But the effectiveness of the drug was hampered by its low aqueous solubility (3.29 ± 0.73 mg/ml), high lipophilicity having log p value ¼ 2.632 ± 0.135 and low bioavailability.

Nanof ormulations are attractive for their potential to improve biopharmaceutic properties of herbal drugs. Solid lipid nanoparticles (SLNs) are colloidal carriers made up of lipids that remain solid at room temperature and body temperature and also offer unique properties such as small size (50–500 nm), favorable zeta potential (i.e. responsible for its stability properties), smooth and spherical shape and less toxic than polymeric nanoparticulate systems as the lipid matrix is made from physiologically tolerated lipid components, which decreases the potential for acute and chronic toxicity. Some other properties of SLNs are the drug pseudo-zero order kinetics and the prolonged/sustained release obtained in vitro for drugs incorporated in SLN (depending upon surface properties). The present study elucidates an attempt to design and characterize a SLN formulation of AD (AD-SLNs), along with the in vitro and pharmacokinetic studies, to improve the oral bioavailability. The antitumor activity was also carried out on Balb/c mice treated with Ehrlich’s ascites carcinoma (EAC) cells.

Materials and methods
Materials
AD (98%) was procured from ChromaDex (Irvine, CA) and Compritol ATO 888 (glycerol dibehenate), Dynaslan 116 (glyceryl tristearate), Dynaslan 114 (glyceryl trimyristate), Precirol ATO 5 (gliceryl distearte) from Gattefosse (St. Priest, France) as a gift samples. Glyceryl monostearate, stearic acid and Tween 80 (polyoxyethylene sorbitan mono oleate) were purchased from Sigma Aldrich (St. Louis, MO). Water was taken from Milli-Q water purification system (Millipore, Billerica, MA). All other chemicals and reagents used were of analytical (AR) grade and procured from Merck (Mumbai, India) and S.D. Fine Chemicals (Mumbai, India). All the components used for the formulation of nanoparticles were pharmaceutically acceptable for oral administration. The MS grade solvents (acetonitrile, methanol, formic acid) used in UPLC-MS method were procured from Merck (Mumbai, India) and S.D. Fine Chemicals (Mumbai, India).

Dulbecco’s modified Eagle’s medium (DMEM), 3-(4,5-dimethylthiazole-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT)
Simultaneous Estimation of Anti-cancer Terpenoids in Pharmaceutical Nanoformulation by RP-HPLC and HPTLC

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Summary. Andrographolide and betulinic acid are the terpenoids having potential anti-cancer activity. The cytotoxicity activity of both the drugs was carried out separately and in combination on liver cancer HepG2 cell lines. High-performance liquid chromatography (HPLC) and high-performance thin-layer chromatography (HPTLC) methods were developed and validated for simultaneous estimation of these two terpenoids as per the International Conference on Harmonization (ICH) guidelines, which was applied for quantification in nanoformulation. The retention time by HPLC and retardation factor by HPTLC for andrographolide and betulinic acid were found to be 2.2 and 6.6 min, and 0.24 ± 0.01 and 0.66 ± 0.01, respectively. Both the methods were validated for accuracy, precision, repeatability, robustness, limit of detection (LOD), and limit of quantitation (LOQ). The content of andrographolide and betulinic acid in nanoformulation was found to be 96.0% and 98.0% by HPLC and 96.59% and 98.33% by HPTLC, respectively, of labelled claim.

Key Words: andrographolide, betulinic acid, high-performance liquid chromatography, high-performance thin-layer chromatography

Introduction

Andrographolide (Fig. 1A), a labdane diterpenoid, is the prime constituent extracted from the leaves of Andrographis paniculata (Burm.f.) Nees. (Acanthaceae) and is responsible for most of its pharmacological properties including anti-cancer activity [1]. Betulinic acid (Fig. 1B), a pentacyclic lupane-type triterpene, is obtained mainly from the outer bark of Betula alba [2] of the family Betulaceae. Both the drugs are reported against several types of human cancers, including neuroblastoma, glioblastoma, medulloblastoma, as well as several carcinomas, i.e., colon, breast, hepatocellular, lung, prostate, and cervix carcinoma [1, 2].
Potential Botanicals for the Treatment of Breast Cancer: Pharmaceuticals Approaches used to Increase the Absorption of Herbal Drugs

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ABSTRACT

Cancer/tumor is an abnormal growth of tissue in which cells proliferate more rapidly than in the tissue from which they came. Breast cancer is the most common cancer in the case of women. Herbs and their secondary metabolites play an important role in anticancer drug discovery. This review deals with some plants/plant constituents (andrographolide, artemisinin, betulinic acid, ellipticine, genistein and green tea polyphenols), which are under clinical or preclinical development for the treatment of breast cancer. They act by inducing apoptosis/cell-cycle arrest, inhibiting angiogenesis, overcoming multidrug resistance (MDR), and/or boosting the immune system. Nanotechnology has been applied to improve drug delivery of herbal drugs and to overcome some of the problems related to drug delivery for cancer treatment. The rationale for combining herbal drugs and nanotechnology for the delivery of herbal drugs is an avenue set to revolutionize the future practice of cancer medicine, and this may well bring on a new dawn of therapeutic strategies.

Keywords: Botanicals, Breast cancer, nanotechniques, novel drug delivery systems
Effect of Andrographolide Solid Lipid Nanoparticles (SLNs) on Breast Cancer

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Andrographolide (AD), obtained from Andrographis paniculata (traditionally known as Kalmegh), is responsible for pharmacological properties like antioxidant, anti-inflammatory, astringent, diuretic, carminative, antihelminthic, antipyretic and anticancer [1]. A diterpenoidal anti-cancer drug andrographolide (1) was encapsulated into SLNs because of poor aqueous solubility, intensely bitter taste and problems of stability under neutral and alkaline conditions [2]. Andrographolide-SLNs (AD-SLNs) were prepared successfully by a solvent injection method and the effect of the drug and its SLNs was studied on a breast cancer cell line. The average particle size of an optimized AD-SLN formulation was 154.9 ± 10.7nm with polydispersity index of 0.203 ± 0.07. AD-SLNs were showing sustained effect with 77.89% drug release in 36h in vitro (2) and 23.78 ± 4.728% cell viability in MCF-7 human breast cancer cell line in ex vivo (3) studies, when compared with standard AD. Encapsulating AD into SLNs may reduce the variability in systemic drug levels and also enable dose reduction, leading to reduced side effects and improvement in biopharmaceutic properties.

Mechanophysical-Chemotherapy Combinations: A Dual Approach to Combat Cancer

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ABSTRACT: Cancer treatment, owing to its myriad limitations, has often been a formidable challenge to both the practitioners as well as researchers. There has been a continued effort in designing newer and successful strategies to obtain optimal results. One such strategy includes the elucidation of a combinatorial approach of the conventional chemotherapy protocol with various mechanophysical methods. This opinion article discusses that how two thrust areas like targeting cancerous cells using a novel drug-delivery system and mechanophysical methods of killing them can be amalgamated into a complete new vector, which is driven with precision, specificity, accuracy, and better efficacy. This approach relies on devising a mechanophysical responsive vehicle, which could be added to other anticancer therapies. The new combined tool would then kill the cancer cells not just by releasing the chemotherapeutic drug at the desired site but also by killing individual cells through the purported mechanophysical stimuli. Summarily, the resultant vector generates an angle influenced by the direction of the mechanophysical vector, leading to a better therapeutic modality.

Key Words: Combination therapies, mechanophysical methods, triggered release systems, physical targeting, vector view

I. INTRODUCTION

Despite the concerted efforts put in by various researchers in designing the different therapeutic modalities, the success rate of certain cancer treatment regimens is only partial, with limited effect on long-term prognosis. Therefore, the scientists have been trying to work out not only new methods but to put the already available ones in combinations that would cure as well as prevent the recurrence of the disease. Conventionally, the whole knapsack of cancer treatments can be redistributed into three packets, namely, surgery, chemotherapeutics, and mechanophysical killing of cancer cells. Different permutations and combinations of the material of these three packets have been tried to achieve the desired response in a patient. The combination is designed with the view that synergistic response of the participants kills the maximum number of cells as well as prevents the recurrence of the problem.