

Nanoencapsulation of Natural Products for Chemoprevention

Imtiaz A. Siddiqui¹, Yogeshwer Shukla^{1,2} and Hasan Mukhtar^{1*}

¹Department of Dermatology, University of Wisconsin, Madison WI, USA

²Indian Institute of Toxicology Research, P.O.Box 80, M.G.Marg, Lucknow, India

Chemoprevention by utilization of natural products has emerged as an important strategy that has the potential to prevent the occurrence of cancer mainly by slowing the process of carcinogenesis. Laboratory data supported by several epidemiological and some clinical studies have validated that bioactive food components produce a broad spectrum of activities that ultimately culminate in prolonging the development time for cancer outcome. With an armamentarium of over 1500 such compounds great hope for cancer control rest on chemoprevention. Despite remarkable effectiveness in preclinical settings, its applicability to human has met with limited success mainly due to inefficient systemic delivery and poor bioavailability of promising chemopreventive agents. Thus, novel strategies are needed to enhance the bioavailability and reduced perceived toxicity associated with the long-term use of potentially useful bioactive food components. We introduced a novel concept of 'nanochemoprevention' where nanotechnology was exploited to augment the outcome of chemoprevention. In our study, we reported significant dose-advantage of polylactic acid-polyethylene glycol (PLA-PEG) encapsulated EGCG, a major polyphenol from green tea (nanoEGCG) over non-encapsulated (native) EGCG. Nano-EGCG exhibited over ten-fold dose advantage for exerting its pro-apoptotic and anti-angiogenic effects in human prostate cancer cells. It is increasingly appreciated that nanoparticle technology could be easily utilized for cancer because of the fact that most of the biological processes occur at nanoscale. Our concept of nanochemoprevention opened a new era in the field of cancer chemoprevention by natural products. Several laboratories worldwide are now focusing their attention on the subject and emerging data is accumulating for use of many agents using diverse nanoparticles. Some other naturally occurring dietary agents which have been tested for chemoprevention following nanoencapsulation are curcumin, resveratrol and taxol. All of these data at present is limited to use in cell culture or xenograft model. Extending this research to in vivo evaluation in well-defined animal bioassay system should be the next step.

Nanoparticles can involve variety of materials like polymers, metals, and ceramics. These particles adopt different shapes and sizes with distinct properties based on synthesis methods and the materials. Over 100 kinds of nanoparticles are under various stages of development and their efficacy evaluation. In general, these are utilized as drug delivery systems, polymer-drug conjugates, polymer microspheres, micelles, and various ligand-targeted products. Several nanotechnology-based constructs are currently in clinical or preclinical development and several of these are already approved by the FDA. 'Nanoencapsulation' is the term generally used where nanoparticles are made featuring a core forming material with a layer of surface modification to enhance the stability and biodistribution and an agent (natural or synthetic) is used as the payload. Nanobiotechnologies have been applied to improve drug delivery and to overcome some of the problems of drug delivery in cancer. Based on the intended use the nanoparticles could be surface modified and conjugated to several moieties for targeted delivery and/or therapy of cancer(s). There are several nanocarrier based drugs in the market ranging from nanoparticulate albumin, liposomes, polymer-protein conjugates etc. which are intended for use against a variety of cancers.

Our proof of principle study on nanochemoprevention demonstrated the usefulness of nanoparticulate technology to enhance the therapeutic effectiveness of natural agents. Our and other studies on the subject suggest that this area of research, though at very early stage is promising. Further, nanotechnology mediated delivery of bioactive food components could also be very effective due to the fact that nanoparticles rarely pose any toxicity to normal cells and is generally biodegradable; therefore, nanoparticles are considered to be safe. Due to these properties nanotechnology could be utilized with considerable advantage over currently employed chemopreventive and chemotherapeutic approaches for cancer. Apart from the nanochemoprevention side of the nanotechnology, studies worldwide have shown that nanotechnology is a plausible approach for cancer diagnosis, imaging and therapeutics. Nanotechnology could be developed as an inexpensive, tolerable and readily applicable approach for cancer control and management. In addition the advancement in nanochemoprevention might help us to achieve the higher concentrations of the phytochemicals which are unattainable when the agents are provided as part of regular diet. There is a little word of caution that the prospective research needs to address the potential long-term toxicity, degradation and metabolism of nanotechnology agents being utilized for integrated imaging, detection and therapy. So far, the results obtained from the nano-encapsulated natural products are very encouraging and their sustained release and improved bio-availability at much lower doses against a variety of cancers are evident. It is imperative to consider that if everything tends to fall in place at the precise interval with nanotechnology and its existing and forthcoming applications for cancer we could expect a success in the near future. For this purpose, the concepts of putting many established agents in some kind of formulation for their stepwise release to target multiple pathways that generally go aberrant in cancer could be very promising and needs to be pursued. Following positive information in animal models that reflect human disease, the concept will need to be verified in human clinical trials.

*Corresponding author: Hasan Mukhtar, Department of Dermatology, University of Wisconsin, Madison WI, USA, Tel: 608 263 3927; Fax: 608 263 5223; Email: hmukhtar@wisc.edu

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