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The 1st Euro-Mediterranean Workshop: Natural Products in Health and Diseases: Cairo, Egypt, March 2, 2015

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ABSTRACT

Natural plant products have been used for centuries for health maintenance and treatment of a variety of diseases in various traditional systems of medicine in Egypt and other African countries, India, China, and other countries around the world. Over the past several decades, the popularity of herbal and other natural products has gradually increased in many western countries. Despite the increasing popularity of natural products, both the public and the professionals are skeptical about the use of these products. Reasons for this skepticism include, but are not limited to, the lack of proper documentation about the source and formulations used; standardization of the composition, batch-to-batch consistency, documented safety of herbal products; and information about the mechanisms of action of these products. The 1st Euro-Mediterranean Workshop: Natural Products in Health and Diseases was organized by the Euro-Mediterranean Association of Life Sciences (EMALS) and various other local organizations to review and discuss the above-mentioned strengths and limitations of the use of natural products. The aim of this workshop was to share best practices and expertise about natural products, and to identify opportunities for collaboration among researchers, health professionals, and business personnel in a productive atmosphere.

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1. Introduction

For thousands of years, natural products have played a very important role in health care and prevention of diseases. The ancient civilizations of the Chinese, Indians and North Africans provide written evidence for the use of products from

natural sources for curing various diseases [1]. The earliest known written document is a 4000-year-old Sumerian clay tablet that records remedies for various illnesses [2]. For example, mandrake was used for pain relief, turmeric for blood clotting properties, roots of the endive plant for gall bladder disorders, and raw garlic for circulatory disorders. These agents are still being used in several countries as alternative medicines.

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According to recent studies conducted by the World Health Organization (WHO), about 80% of the world's population relies on traditional medicine [3]. About 121 drugs prescribed in the USA today are from natural sources, 90 of which are derived either directly or indirectly from plant sources [4]. Furthermore, forty-seven percent of the anticancer drugs in the market are from natural products or natural product mimics [4].

It is well documented that most natural products are enriched with bioactive components that have protective action against potentially disease-inducing events. There is currently a growing body of evidence that supplementing the human diet with natural products offers major benefits for human health and well-being. The use of complementary/alternative medicine, functional foods, and other natural products has been increasing rapidly worldwide, mostly because of the perceived safety of such products. The issues regarding the efficacy and safety of currently available modern (allopathic) drugs have prompted the search for safer and more effective alternatives. As elaborated below, this workshop was focused on the use of natural products for health and disease prevention.

The aim of the 1st BioNat International Workshop was to share best practices and expertise, and to identify opportunities for collaboration. Well-known researchers, health professionals, and business personnel presented their expertise in a productive atmosphere. It was organized by the Euro-Mediterranean Association of Life Sciences (EMALS) and various other local organizations. EMALS aims to contribute effectively to the development of international and national programs of scientific research; to provide strategic services that affect the lives of scientists, biomedical researchers and their assistants; to develop their professional and research competence; and to enlist their participation in increasing the awareness of various segments of the society about science in general and natural products in particular.

The above-mentioned BioNat workshop considered a range of issues, such as (1) classification and distribution of wild medicinal plants in Egypt; (2) separation and identification of bioactive compounds from plants; (3) natural products in the prevention and treatment of human diseases; (4) antimicrobial activity of natural products; (5) search for microbial sources of natural and unnatural products; (6) natural products chemistry, chemosystematics and quality control; and (7) patentability in pharmacognosy, plant extraction and dietary supplements.

To begin with, Dr. Ashraf A Khalil introduced the speakers, presented a brief synopsis of the importance of the workshop and discussed the day's program in detail. During the period of this workshop, the participants met with experienced professionals from diverse disciplines, but all connected with natural products research and applications. Thus, professors, project leaders of R&D, post-doc researchers, CEOs, technical managers, heads of departments, group leaders, PhD students, and research scientists from both developed and developing countries were brought together on this occasion to share current knowledge and future strategies for the use of medicinal and herbal products for the prevention and treatment of human diseases.

The format of the workshop consisted of lectures and discussions aimed at reviewing and exchanging basic information about herbal products and their use in different diseases, and sharing information via a questionnaire completed by the par-

ticipants. The titles of lectures, the names of the presenters, and the abstracts summarizing the major findings are given below. A copy of the questionnaire is also enclosed. The responses to questions were read, analyzed, and utilized to guide the discussions within and between lectures.

2. Presentations

2.1. Nanoencapsulation of natural products for their enhanced anti-cancer activity

The introductory lecture was presented by Prof. Hasan Mukhtar (School of Medicine and Public Health, Department of Dermatology, University of Wisconsin, Madison, WI, USA). He enlightened the participants with the information that the practical applicability of the bioactive food components for the prevention and treatment of human cancer has met with limited success largely due to inefficient systemic delivery and bioavailability of promising agents despite highly encouraging results in preclinical settings. His group was the first to employ nanotechnology to improve the outcome of cancer chemoprevention by natural agents and to introduce the concept of, as well as the term, *Nanochemoprevention* [5]. To establish the proof-of-principle, they encapsulated epigallocatechin-3-gallate (EGCG) in PLA-PEG nanoparticles (NPs) and demonstrated a ten-fold dose advantage over native EGCG in human prostate cancer (PCa) cells both *in vitro* and *in vivo*. Later, they reported the efficacy assessment of a nanotechnology-based oral formulation of chitosan NPs encapsulating EGCG in a PCa tumor xenograft mouse model. Prof. Mukhtar's lab demonstrated that nanoformulated EGCG significantly induced apoptosis and reduced the expression of markers of cell proliferation in the tumors [6]. Recently, they proposed targeted NPs as novel prototypes for the delivery of EGCG, thereby exploiting small molecular entities able to bind to prostate-specific membrane antigen (PSMA). PSMA-specific cellular binding and uptake of the nanosystems were detected, and EGCG polymeric NPs showed an increased anti-proliferative activity in both PSMA-negative and PSMA-positive PCa cells, with better efficacy in PSMA-positive cells. The study revealed a better response to targeted NPs in inhibiting the tumor growth as compared to non-targeted EGCG. In a parallel study, the team of Prof. Mukhtar tested the efficacy of EGCG encapsulated in chitosan NPs and surface-functionalized with A10 2'-fluoropyrimidine RNA aptamers (chit-EGCG-Apt) that recognize the extracellular domain of PSMA. They detected PSMA-specific internalization and accumulation along with a sustained and constant release of EGCG from the nanobioconjugates. Chit-EGCG-Apt also led to a PSMA-specific enhanced anti-proliferative activity in PCa cells with a significant decrease in IC_{50} . EGCG encapsulated in chit-EGCG-Apt also retained its mechanistic identity for induction of apoptosis, modulation of cell cycle, and inhibition of invasion and migration. They also designed novel polymeric NPs composed of PLGA-PEG-COOH encapsulating resveratrol (nano-RSV) to enhance its bioavailability and to improve the intracellular penetration. These NPs were able to control the RSV release at both acidic and physiological conditions. Fluorescence microscopy revealed that NPs were efficiently taken

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