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Review Article

Modulation of dendritic cell immune functions by plant components

Alia M. Aldahlawi[a,b,*]

[a] Department of Biological Sciences, Faculty of Sciences, King Abdulaziz University, Jeddah, Saudi Arabia
[b] Immunology Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah, Saudi Arabia

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ABSTRACT

Dendritic cells (DCs) are the key linkage between innate and adoptive immune response. DCs are classified as specialized antigen-presenting cells that initiate T-cell immune responses during infection and hypersensitivity, and maintain immune tolerance to self-antigens. Initiating T-cell immune responses may be beneficial in infectious diseases or cancer management, while, immunosuppressant or tolerogenic responses could be useful in controlling autoimmunity, allergy or inflammatory diseases. Several types of plant-derived components show promising properties in influencing DC functions. Various types of these components have been proven useful in clinical application and immune-based therapy. Therefore, focusing on the benefits of plant-based medicine regulating DC functions may be useful, low-cost, and accessible strategies for human health. This review illustrates recent studies, investigating the role of plant components in manipulating DC phenotype and function towards immunostimulating or immunosuppressing effects either *in vitro* or *in vivo*.

1. Introduction

Dendritic cells (DCs) are professional antigen-presenting cells that provide a link between the innate and the adaptive immune responses. DCs stimulate adaptive immune response by activating T lymphocytes, inducing an effector response or tolerance depending on the DC differentiation level. In addition, DCs play a crucial role in immunosuppression and maintain tolerance against self-antigens. Therefore, DCs have become a key target for research activities focused on manipulating DCs to obtain novel biological modifiers that can be used for the treatment or management of different infectious and immune-related diseases. Herbal plants offer a wide range of medicinal components that have proved beneficial in treating different diseases worldwide.

Several plant-derived components may have immunostimulatory, immunosuppressive, and/or anti-inflammatory activities depending on the plant type and extraction method. Most of these therapeutic plants may be effective in modulating DC activities and considered as an alternative tool for treatment. Therefore, I present the findings of recent studies investigating the role of plant components in manipulating DC functions either *in vitro* or *in vivo*.

2. Modulation of DC activities

DCs are a heterogeneous population of immune cells, comprising different subsets that can be distinguished by their phenotypic and functional properties. Functional properties include the ability to upregulate specific

* P.O. Box 80200 Jeddah, 21589, Saudi Arabia.
E-mail address: aaldahlawi@kau.edu.sa (A.M. Aldahlawi).

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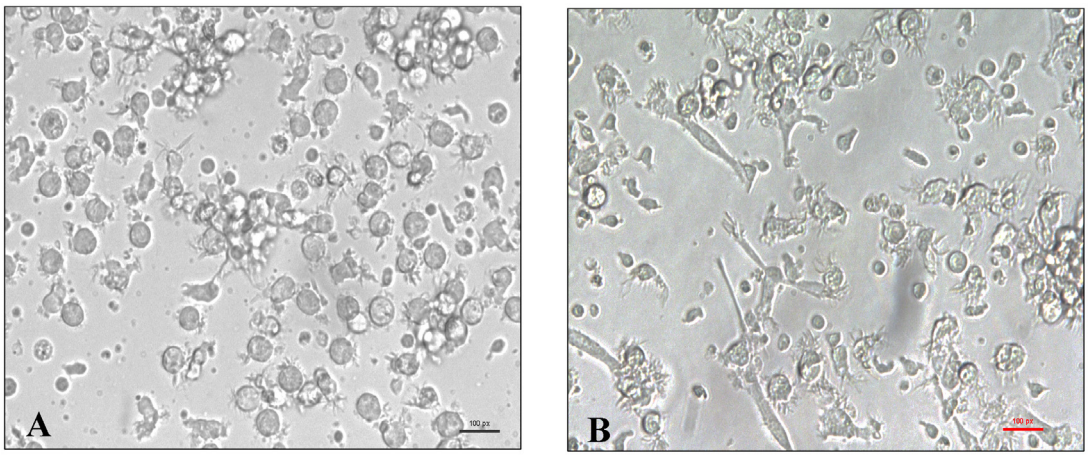

Fig. 1. (A) Morphology of immature DCs generated from peripheral blood monocytes cultured in RPMI-1640 medium supplemented with granulocyte–macrophage colony-stimulating factor and interleukin-4 for 7 days. (B) Immature DCs stimulated with 1 μg/mL lipopolysaccharide for 24 hours showed long cytoplasmic veils typical for mature DCs. Cells were photographed using a digital camera assembled on a bright field inverted microscope. Original magnification was 40×. (Unpublished data, Immunology Unit, King Fahad Medical Research Center, KAU, Jeddah, Saudi Arabia.).
DC = dendritic cell.

maturation markers and the capacity to stimulate naïve T cells. The maturation status of DCs may be responsible for either induction of immunity or tolerance. The process of DC maturation is highly regulated and results in conversion of immature DCs in the periphery into fully competent antigen-presenting cells. During conversion, DCs undergo a number of phenotypical and morphological changes (e.g., formation of dendrites; Fig. 1). In addition, there are reallocation of major histocompatibility complex (MHC) molecules from intracellular endocytic compartments to the DC surface; downregulation of antigen internalization; an increase in the surface expression of co-stimulatory molecules; cytoskeletal reorganization; secretion of chemokines, cytokines, and proteases; and surface expression of adhesion molecules and chemokine receptors [1,2]. This process can be induced by a variety of infectious agents, cytokines, and natural products. Several researchers have studied the impact of various natural product extracts during the recent years.

2.1. Plant components modulating DC differentiation and maturation

Different types of plants and plant components were shown to induce DC differentiation either *in vitro* or *in vivo* including pinecone extract [3], the traditional Japanese herbal plants kampo and Hochu-ekki-to (HOT) [4], and the water soluble extract of fern *Polypodium leucotomos* named Anapsos [5]. Anapsos especially was found to enhance production of interleukin (IL)-1α, IL-1β, and tumor necrosis factor α proposing a stimulation of monocytes and DCs *in vitro*. In addition, *Astragalus mongholicus* polysaccharide isolated from one of the Chinese herbs was found to enhance the co-expression of CD-11c and MHC class II molecules on murine bone marrow (BM)-derived DC (BMDC) surfaces, reduce fluorescein isothiocyanate–dextran uptake, and produce a higher level of IL-12 than untreated DCs, suggesting that it modulates DC maturation [6].

Moreover, some plant components were reported to induce both the differentiation and maturation of DCs *in vitro*, such as lupane acetate of cortex periplocae [7], the aqueous and organic fractions from *Petiveria alliacea* [8], acidic polysaccharide isolated from ginseng (*Panax ginseng* Meyer) [9], and *Lycium bararum* polysaccharide (LBP) extracts [10]. One interesting study on LBP demonstrated its ability to induce phenotypic and functional maturation of DCs [11]. The therapeutic effects of LBPs were related to their ability to induce DC maturation through Toll-like receptor (TLR)2- and/or TLR4-mediated nuclear factor (NF)-κB signaling pathways [12]. Likewise, *Achyranthes bidentata*, a traditional Chinese medicine also provides phenotypic and functional maturation of murine DCs, suggesting that it may be used to boost immune responses [13]. Similarly, the polysaccharide obtained from a Chinese medicinal herb, Zhu Ling [the sclerotium of *Polyporus umbellatus* (Per) Fr], was found to induce the activation and maturation of murine BMDCs through TLR4 [14].

Some plant extracts were found to interfere with DC differentiation and maturation, as shown by the exposure of monocytes to areca nut extracts. These extracts did not effect the expression of HLA-DR and CD11c, but markedly decreased the proportion of CD40-positive cells, expression of CD86, and IL-12 production. Curcumin was found to induce an immunosuppressant effect on DCs and prevent response to lipopolysaccharide (LPS) by blocking of maturation markers, cytokines, chemokine expression, and endocytosis [15]. Moreover, fisetin, a flavonoid commonly present in fruits and vegetables, in addition to TongXinLuo, *Semen cuscutae*, and *Acanthopanax koreanum*, a traditional Chinese medicine, impair functional maturation of DCs [16–19]. Acetylcorynoline component derived from *Corydalis bungeana* herbs was also reported to work as a potent immunosuppressive agent through its ability to alter of DC maturation and function [20].