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Natural compounds, a large majority coming from plant origin, have enormously contributed as immunomodulatory therapeutics. Since ancient times, natural medicines have always fascinated the humans, with their own qualities of harmless treatments with minimal side effects. There are thousands of natural compounds such as the compounds from plants like *Curcuma longa*, *Viscum album*, *Allium sativum* (garlic), and *Calendula officinalis* and their derivatives which are known to influence the immune system either by affecting the functions of immune cells like dendritic cells, macrophages, lymphocytes, and natural killer (NK) cells or by affecting the antibody secretion to control the infection and to maintain the immune homeostasis.

Immunomodulatory functions of these compounds include immunostimulation by activating the immune cells and increasing the proliferation of lymphocytes and secretion of immunostimulatory cytokines such as IL-1, IFN-, IL-6, IL-12, and anti-inflammatory effects by inhibiting the proinflammatory cytokines and inhibiting the cellular activation and proliferation. Immunomodulatory functions also include the role of these natural compounds in regulating the immune responses by interfering with the tolerance mechanisms, thereby establishing an immune homeostasis. Therefore, it is interesting to dissect the immunomodulatory mechanisms of natural compounds and to discover the novel promising candidates that can be used in the future immunotherapeutic strategies.

An extensive future investigation is required with respect to their mechanisms of action at systemic, cellular, and molecular level to extend up to broad-spectrum clinical trials. Given the multiple biological effects of natural compounds, it is exceedingly interesting to design the future therapeutic strategies for inflammatory pathologies and malignant diseases with a synergistic combination of natural products together with various conventional therapies.

This special issue therefore is focusing on such natural immunomodulators, in order to provide the maximum proof of concept for their use, as natural medicines.

Potential topics include but are not limited to the following:

- Identification of unknown novel therapeutic molecules or products of natural origin and their documentation
- Identification of novel biological effects of known therapeutic natural compounds
- Effects of natural compounds on the activation, cytokine secretion, and T cell stimulatory effects of dendritic cells and macrophages
- Effects on activation and functions of basophils, eosinophils, and natural killer cells
- Effects on T cell activation, proliferation, cytokine secretion, and T cell polarization
- Effects on B cell activation, functions, and antibody secretion
- Effects on the functions of regulatory T cells and immune tolerance
- Antitumor properties of natural compounds
- Effects on immune system during antitumor mechanisms
- Anti-inflammatory properties of natural compounds on LPS induced inflammation
- Molecular mechanisms and signaling pathways underlying these immunomodulatory effects
- Studies on animal models and human cohorts
- Combinational therapeutic approaches with natural compounds and other conventional therapies

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