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The most important Iranian medicinal plants with immunomodulatory property according to traditional medicine and modern research findings Ali Sheikhian¹, Sadegh Rezapour², Hedayatollah Shirzad^{3*}

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ABSTRACT

Innate immunity is the body's first line of defense against different pathogenic agents. Macrophages and neutrophils are two main cells that contribute significantly to innate and acquired immune responses, and important effector cells to destroy harmful agents. Function of these cells can be modulated by natural and synthetic compounds. Nowadays, the immunomodulatory effects of herbal plants is a hot research issue worldwide as a good candidate to strengthen immune system. The aim of this review article is to report the most important medicinal plants of Iran with immunomodulatory effect. The search terms including immunomodulatory, medicinal plants, and Iran were used to search for relevant articles in some national databases such as Scientific Information Databases, and Google Scholar search engine. Thyme, Pennyroyal, Garlic, Echinaceae and Olive were found to be traditionally used to strengthen the immune system of the body. Aloe (Aloe barbadensis), Palm (Phoenix ductylifera), Fennel (Foeniculum Vulgare) and Cumin seed (Cuminum cyminum) have been reported to have immunomodulatory effects according to scientific research.

KEY WORDS: Immunomodulatory, medicinal plants, Iran.

1. INTRODUCTION

Infectious and non-infectious diseases are day by day increasing in prevalence. Epidemiological studies have highlighted detection of disease course and strategies of disease prevention and management (Delfan, 2014; Bahmani, 2015; Bahmani, 2016). The body response to different infectious diseases depends on how the immune system reacts against the corresponding agents and whether this system is able to do so or not. Therefore, the factors that affect the immune system can significantly influence the outcome of the disease processes (Li and Brown, 2009, Azadmehr, 2011, Gupta, 2016). Innate immunity is the body's first line of defense against different pathogenic agents. This system consists of soluble factors and phagocytic cells such as macrophages and neutrophils that contribute significantly to inductive and effector phases of immune responses. The specific or acquired immunity functions to direct or amplify innate immunity (Ghazanfari, 2006; Gao, 1993). It has also an important role to fight the foreign invaders. Today, some researchers focused on the use of medicinal plants as potential immunomodulatory agents to potentiate immunity or direct the response toward a better outcome (Hassan, 2003; Ghazanfari, 2002).

Herbal substances which are used in traditional medicine have long been paid attention (Baharyand-Ahmadi, 2015; Parsaei, 2016; Amirmohammadi, 2014, Saki, 2014). Currently, with regard to different side effects and disadvantages of synthetic substances, the use of natural substances is considered as a good alternative to boost the immune system and treat different diseases (Asadi-Samani, 2014; Bahmani, 2014; Bahmani, 2015; Ebrahimie, 2015). Regarding the significance of the medicinal plants that strengthen the immune system of the body, the aim of this review article is to report the most important medicinal plants of Iran with immunomodulatory effects.

2. MATERIALS AND METHODS

In this work, the search terms including immunomodulatory, medicinal plants, and Iran were used to search for relevant articles in some national databases such as Scientific Information Databases (SID) and scientific search engines such as Google Scholar and national databases such as PubMed.

3. RESULTS

According to the references of Iranian traditional medicine, the following plants can strengthen immune system:

Thyme: Thyme extract stimulates and strengthens the immune system (Mosayebi, 2009).

Green tea: Polyphenols of Green tea boost immunity of the body (Mosayebi, 2009).

Echinaceae: Boiled echinacea has long been used to strengthen the immune system, and to prevent and treat common cold and influenza. This plant is recommended for attenuating nasal congestion and reduction of nasal discharge (Mosayebi, 2009).

Pennyroyal: Pennyroyal essential oil enhances the immunity of the body (Mosayebi, 2009).

Allium sativum: Allicin and thiosulfate of A. sativum help the body fight against pathogenic agents and can stimulate the immune system of the body (Mosayebi, 2009).

Foeniculum Vulgare: Foeniculum Vulgare Mill leaf extract stimulates the defense system of the body and helps it to fight pathogenic agents (Mosayebi, 2009).

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38 studies identified via electronic search in SID, Google Scholar and etc. 2 studies identified via manual search in references and experts' guide. 7 studies identified after removing duplicate publications and irrelevant studies 16 studies screened 14 studies assessed for eligibility 2 studies excluded (including articles

without English abstract in the electronic databases, etc.)

Figure. Flowchart of the review article

Table 1 Medicinal	nlants of Irai	n with immunom	adulatory effects
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Scientific name	Family	Persian name	Effects	
Aloe barbadensis	Liliaceae	Sabre- Zard	Treatment of male C57BL/6 mice under immunization with 120 mg of <i>A. barbadensis</i> extract for 25 days caused a significant decrease in the clinical symptoms of experimental autoimmune encephalomyelitis and delay in the onset of disease. Tumor necrosis factor alpha production by mononuclear cells in the spleen decreased significantly in the mice treated with <i>A. barbadensis</i> compared to control group (Mosayebi, 2009).	
Phoenix ductylifera	Palmaceae	Khorma	A study investigated the prophylactic and therapeutic effects of <i>Punica</i> granatum juice and <i>Ficus carica</i> and <i>P. dactylifera</i> fruits on acute colitis in rats using interleukin-6 and tumor necrosis factor as variables. Immunological findings demonstrated that intake of <i>P. granatum</i> juice alongside <i>P. dactylifera</i> for two months decreased interleukin-6 production and had with anti-inflammatory and immunomodulatory effects (Zangeneh, 2012).	
Foeniculum Vulgare Mill	Apiaceae	Razianeh	A study demonstrated that the production of nitric oxide increased significantly by peritoneal macrophages treated with 10 mg/mL of acetonic <i>F. vulgare</i> extract, which may confirm the immunomodulatory effects of <i>F. vulgare</i> (Sampedro, 2004).	
Cuminum cyminum	Apiaceae	Zireh- Sabz	The survival of macrophages and the production of nitric oxide were lowered by 50 and 500 μ g/mL of <i>Cuminum cyminum</i> essential oil compared to control group. MTT assay demonstrated that 5 and 500 μ g/mL of essential oil caused a marked inhibition of tumor cells and exerted an immunomodulatory effect (Naeini, 2009).	

4. DISCUSSION AND CONCLUSION

A. barbadensis has antiulcer, antioxidant, antidiabetic, anti-inflammatory, and anticancer effects (Langmead, 2004; Muller, 2003; Sosa, 2007; Akev, 2007; Rajasekaran, 2005; Benedi, 2004). Medicinal plants contain bioactive and pharmaceutically effective compounds, antioxidants, flavons, flavonoids, phenols, anthocyanins, and tannins (Farkhondeh, 2016). Many of the pharmaceutical effects of these plants are due to the pharmaceutically bioactive compounds (asadbeigi, 2014; Karamati, 2014). Anthraquinone is the main compound of *A. barbadensis* (Vinson, 2005). *P. dactylifera* has antioxidant and antimutagenic effects (AI-Shahib and Marshall, 2003). *P. dactylifera* contains nicotinic acid, folic acid, palmitic acid, linoleic acid, linolenic acid, and oleic acid (Parker, 2002; Salehi Surmaghi, 2006). In traditional medicine, *F. vulgare* is used as carminative, antispasmodic, antiseptic, and inhibitor of breast milk production. Trans-anethole, limonene, and fenchone are some of the effective compounds of *F. vulgare* fruit (Zargari, 1997). *Cuminum cyminum* is traditionally used to treat epilepsy, diarrhea, and toothache with antithrombotic and antioxidant effects as some traditional effects of this plant according to traditional medicine (Srivastava, 1989; Gagandeep, 2003).

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