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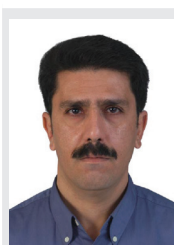
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# Parsley and immunomodulation

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**“Although parsley has been used to treat allergy, autoimmune and chronic inflammatory disorders, the mechanism underlying its beneficial effects in these immune-mediated diseases have been rarely investigated.”**

Throughout history, herbs have been utilized as an important constituent of foods, industry and folk medicine. One of the widely used vegetal species in various nations' medicine is parsley (*Petroselinum crispum*), which has remedial effects as a powerful diuretic agent [1,2], an abortifacient [3–5] and an expectorant [6,7]. Parsley is a native herb of the central Mediterranean region (southern Italy, Algeria and Tunisia), which is in the Apiaceae family, and is a species of *Petroselinum* [8].

It is believed that parsley is one of the world's seven most potent disease-fighting spices [8]. Although parsley has been used to treat allergy, autoimmune and chronic inflammatory disorders, the mechanism underlying its beneficial effects in these immune-mediated diseases have been rarely investigated. Of the various therapeutically beneficial aspects of parsley, we decided to examine the immunomodulatory effects of this plant.

In our study, the effects of parsley essential oil on phytohemagglutinin (PHA)-stimulated splenocytes (T cells) and lipopolysaccharide (LPS)-stimulated B cells, as the main effector cells in adaptive immune system, was examined. In addition, the suppressive activity of different concentrations (0.01–100 µg/ml) of parsley essential oil on macrophages and LPS-stimulated macrophages for evaluation of nitric oxide (NO) was studied [9]. The methyl tetrazolium method was performed to survey the proliferation of mitogen-stimulated splenocytes as well as the viability of pretreated macrophages [9]. NO

production of both macrophage groups was determined in the Griess reaction [9]. Parsley essential oil suppressed the proliferation of PHA-stimulated splenocytes at all applied concentrations. Similarly, it had a suppressive effect on the unstimulated and LPS-stimulated splenocytes, but only at high concentrations (10 and 100 µg/ml). NO production by unstimulated and stimulated macrophages was reduced by parsley essential oil; although, in all concentrations, unstimulated ones produced lower amounts of NO compared to the control group. These results can propose the suppressive effect of parsley essential oil on macrophages, as the major cells involved in the innate immune system [9].

The use of immunosuppressive drugs to control unwanted immune responses such as allergies, autoimmune disease and transplant rejection has grown over the past few years. The disadvantages and side effects of any immunosuppressive treatment are a significant and growing anxiety [10]. Some serious side effects including nephrotoxicity, hepatotoxicity, induction of diabetes, hypertension and neurotoxicity have been stated for various immunosuppressive drugs [10,11]. Thus, healthier and lower risk therapeutics are required. In this regard, more attention has been recently made on natural products. For example, the immunosuppressive activity of various herbal plants and ingredients including *Achillea talagonica*, [12] *Plantago ovata* [13], *Boerhaavia diffusa* [14], *Stachys obtusirena* [15], *Pollen Typhae* [10] and *Silymarin* [16] has been explored.

Parsley has also been shown to possess other biological activities than these described here. Several studies have suggested anticancer potential of parsley. By means of ascorbic acid-induced lipid peroxidation, the antilipoperoxidant activity of parsley extracts has been shown [10,17,18]. The antioxidant activity of parsley essential oil has been confirmed in other investigations. Wong *et al.* indicated that the phenolic compounds of parsley were responsible for its antibacterial and antioxidant activity [19]. Zhang and his coworkers demonstrated the antioxidant activity of this herb in terms of  $\beta$ -carotene bleaching capacity and free radical scavenging activity [7]. This concept was then supported by further studies [20].

Parsley possesses several flavonoids such as apiin and luteolin, and its essential oil contains apiol and myristicin. These components are believed to be responsible for the therapeutic effects of parsley [17,21]. Kandaswami *et al.* indicated the direct and indirect effects of flavonoids on tumor cells. Their studies showed that the hydroxylation pattern of the B-ring of the flavons and flavonols, such as luteolin and quercetin, seemed to affect their angionesis and anticancer activity, especially the inhibition of protein kinase activity and antiproliferation [22].

Robak and his coworkers believe that flavonoids are the superoxide anion scavengers of the media and this effect can also lead to their anti-inflammatory effects [23].

Daly *et al.* observed bioactive phytochemicals, including carotenoids, in parsley [6]. Carotenoids were shown to be associated with a low risk of several human chronic disorders including age-related macular degeneration and certain cancers.

Matching the wide use of this vegetal species as a diuretic in folk medicine, natriuretic and hypotensive effects of parsley were demonstrated in studies by Kreydiyyeh and Usta, and de Campos *et al.* [1,2]. Further studies indicated more biological effects of parsley plants, such as provitamine A activity, and influencing the cell signaling pathways [22,23].

In summary, parsley is a plant with various biological activities. With respect to its immunomodulatory effects, we found that its inhibitory effect on PHA-stimulated splenocytes might be due to the production of cytokines such as IFN- $\gamma$  and IL-2, which are vital for T-cell proliferation or it may influence the signaling pathways. Our results indicated that parsley essential oil can modulate the activity of macrophages without exerting cytotoxic effect. The immunomodulatory effect of parsley essential oil and its modulatory effects on NO production and function of macrophages may identify it as a useful natural candidate to treat some autoimmune and allergic diseases; however, its further application needs more investigation.

#### Financial & competing interests disclosure

*The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

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