

Effect of Intake of Mate on the Parkinson's Disease

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Objective of the Study

The aim of this study is to determine whether Yerba Mate is able to protect dopaminergic neurons in the substantia nigra, a structure particularly sensitive to inflammation that is involved in Parkinson's disease.

Summary of the Work Plan

In order to induce dopaminergic neuronal damage, we will use the Parkinson's disease *in vitro* model (using the N27 dopaminergic cell line), several molecular techniques will be used in order to evaluate the anti-inflammatory and neuroprotective potential of yerba mate. Hence, this herb will be administered to cells treated with MPP+ and the protective effects of this treatment will be evaluated.

Introduction

Parkinson's disease (PD) is a neurodegenerative disorder related to age that is characterized by the progressive degeneration of nigrostriatal dopaminergic neurons of the substantia nigra pars compacta [1]. This leads to motor dysfunction of the extrapyramidal system, which is accompanied by cognitive dysfunction, progressive loss of autonomy and mood alterations [1-3]. Although several genes have been identified as responsible for some types of early onset familial PD [4], the aetiology of the disease remains unknown. Several factors, such as oxidative stress, mitochondrial dysfunction, reduced trophic factors, alterations in the ubiquitin proteasome system and neuroinflammatory mechanisms, seems to cooperate in the progressive death of neurons in the SNpc [1,3,5-10]. Accumulating evidence suggests that inflammation may play a central role in the cell loss that occurs in PD. Hence, several authors have shown the existence of activated microglia in the SN of PD patients [7,11], which is accompanied by an increased expression of inflammatory cytokines [12,13]. Moreover, it has been shown that inflammation is present in different animal models of PD, including those produced by toxins such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), 6-hydroxydopamine (6-OHDA) or rotenone [14-17]. In fact, epidemiological studies have shown that the incidence of idiopathic PD is about 50% lower in chronic users of nonsteroidal anti-inflammatory agents or cyclooxygenase inhibitors with respect to non-users [18-20].

Although the cause of the disease is unknown, there are various known risk factors that may increase the likelihood of developing the disease, which include age, sleep disorders, brain trauma and exposure to certain environmental factors such as pesticides and herbicides and some nutritional habits [21-24]. Yerba mate is a widely used tea herbs in many countries as Brazil, Argentine, and many Mediterranean countries as Syria [25]. Where is the yerba mate could be considered as the unique or most popular traditional drink as in my town and my region in Syria, which is the mountains fronteering with Lebanon, called Kalamoun mountains. I realized after my study of doctoral thesis, which was about the effect of metformin on Parkinson's disease [26], that there is rarely or nearly no evidence of PD or Alzheimer's diseases in this region. I looked in scientific references and I confirmed this idea by many other related articles that study the neuroprotection and anti-inflammatory effects of this herb. Hence, it has been described the positive effect of mate on breast cancer [27], the effect of phenolic compounds of mate on inflammatory and oxidative biomarkers in HIV/AIDS individuals [28], its anti-inflammatory effect in a murine model of pleurisy [29], its anti-obesity effect [30] and its effect on muscle strength [31]. Moreover, in a recent paper, Gatto, *et al.* [25] have shown an inverse association between yerba mate consumption and idiopathic PD. All these studies confirm that mate has a special positive effect in prevention and alleviation of diseases related to oxidative stress, inflammation and maybe more unknown factors. Given the anti-inflammatory activity of mate and the importance of neuroinflammation in the development of PD, the aim of this study is to determine whether intake of this herb infusion is able to protect dopaminergic neurons in the SNpc using an *in vitro* model of PD based on the treatment of N27 differentiated culture.

Expected Results

Taken into account the anti-inflammatory properties described for yerba mate, it is highly possible that treatment with this herb protect dopaminergic neurons from the treatment with MPTP. PD is the second most prevalent neurodegenerative disease affecting approximately 1 - 3% of the population. The results of these experiments could provide new and interesting neuroprotective strategies based on consumption of a plant easily and widely used. The use of mate could help lots of people to come over many problems which they face at each stage of their life, and maybe to rebuild new systems of diet at public level. Besides to all mentioned positive effects of this herbal infusion it is a so famous drink for students as it has anxiolytic, stimulant and neuroprotective effects and even to relieve pain which may be caused by several factors [32]. These effects are potentially modulated by the cholinergic system as well as by caffeine [33-37].

Suggested continuations of this project

The Parkinson's disease *in vivo* model bases on the treatment with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), (using C57BL mice). Combination of several molecular and histochemical techniques will be used in order to evaluate the anti-inflammatory and neuroprotective potential of yerba mate. Hence, this herb will be administered to animals or cells treated with MPTP and the protective effects of this treatment will be evaluated.

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