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THE EFFECT OF GINKGO BILOBA ON ALZHEIMER'S DISEASE

by

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Thesis submitted in partial fulfillment
of the requirements for the degree

of

DEPARTMENT HONORS

in

Nutrition and Food Science

Approved:

Thesis/Project Advisor

Department Honors Advisor

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UTAH STATE UNIVERSITY
Logan, UT

2002

The Effect of Ginkgo Biloba on Alzheimer's Disease

Abstract. Alzheimer's disease is a progressive dementia associated with increasing loss of memory, intellectual function, and disturbances in speech. It is the most common form of dementia. It is an incurable disease and has four stages which culminate in coma and death. The average survival rate for Alzheimer's is seven years. Presently, the only treatments approved in the United States for Alzheimer's are the drugs tacrine and donepezil. These drugs improve cognitive function in early Alzheimer's. However, Ginkgo biloba has recently been looked at as another treatment option and has been approved for use in Germany. Ginkgo Biloba was originally used in China and has recently become popular in the western world. It claims to improve cerebral insufficiency, hearing impairment, circulation to the extremities, and memory in early Alzheimer's disease. The side effects of Ginkgo include reduced blood clotting; restlessness, diarrhea, nausea, headache, dizziness, and heart palpitations in less than four percent of people; and it isn't recommended for pregnant or lactating women. Several studies have been conducted to investigate the effects of ginkgo biloba. These studies found a protective effect against free radical damage, a beneficial effect on neural cells, and similar effects of ginkgo when compared to tacrine. Despite the positive findings for ginkgo biloba in these studies, it is limited by only having benefit in the early stages of Alzheimer's disease. The findings for ginkgo biloba support its use in early Alzheimer's, but more research needs to be done before it can be recommended for treatment in the United States.

Introduction

One of our greatest fears as a people is losing mental capacity as we age. Loss of mental capacity is more commonly called dementia, and the most common form of dementia in the United States today is Alzheimer's disease. This progressive dementia is named after Alois Alzheimer, who first described the clinical findings related to it, and it affects fifteen million people worldwide(5). The Merck Manual of Diagnosis and Therapy defines Alzheimer's disease as "A progressive, inexorable loss of cognitive function associated with an excessive number of senile plaques in the cerebral cortex and subcortical gray matter, which also contains beta amyloid and neurofibrillary tangles consisting of tau protein."(p 1395-6) Patients afflicted with Alzheimer's have a progressive loss of memory, intellectual function, and increasing speech disturbances. Incidence increases as age increases, with most cases appearing after the age of

sixty(2). There is no known cause of Alzheimer's disease, although there is thought to be a common genetic factor(5). Risk factors commonly associated with Alzheimer's disease include birth order, head injury, level of education, and presence of Down's syndrome(5).

Stages of Alzheimer's

Alzheimer's disease presents itself in four stages. The first stage is called the early stage, and is characterized by loss of recent memory, inability to learn and retain new information, language problems, mood swings, and personality changes(2). Language problems generally include anomia (forgetting names of objects), echolalia (repeating words spoken by others), and agnosia (loss of comprehension)(5). In the early stage sociability isn't lost, but families may report strange behavior. The next stage is called the intermediate stage, and it is characterized by loss of long-term or remote memory, assistance required for basic activities such as bathing and toileting, and behavioral disorganization such as wandering, agitation, hostility, uncooperativeness, and physical aggression(2). By this point patients have lost all sense of time and place and get lost and confused easily. The next stage of Alzheimer's is the severe stage. By this stage, patients have lost all memory, cannot walk, eat or perform any activity of daily living. Patients become at risk for pneumonia, malnutrition, and pressure sores and often must be placed in a long-term care facility(2). The patient eventually becomes mute and proceeds to the end stage of Alzheimer's, which is characterized by coma and death(2).

Current and Potential Treatments

The current treatment for Alzheimer's in the United States is limited to tacrine and donepezil, two drugs that are supposed to improve memory in the early stage of Alzheimer's disease(4). However, a new treatment may be up for consideration. In 1994, a new treatment was approved in Germany. This treatment is SeGb, an extract of the Ginkgo Biloba tree(4).

Extracts of this tree's leaves have been used in China for various conditions since 2800 BC. It has only recently become popular in the western world(3).

Ginkgo has a variety of health claims associated with its use. It is supposed to reduce cerebral insufficiency (forgetfulness, dizziness, concentration difficulties, memory impairment, depression, anxiety), reduce tinnitus and other hearing impairment, improve circulation to the extremities, and improve memory in early Alzheimer's disease or other multi-infarct dementia(3). It is this last claim which has recently been the subject of several studies involving tests of Ginkgo Biloba extract. In the following studies a standardized extract of Ginkgo containing 24% flavonoid glycosides and 6% terpenoids was used. This extract will be referred to as EGb 761(1).

In a study comparing EGb 761 to tacrine in patients with light to moderate dementia, EGb 761 patients showed similar central nervous system improvements as those patients using tacrine. The patients were evaluated using computer-analyzed electrical activity of the brain. 240 mg of EGb 761 were used in treating the dementia patients in comparison with 40 mg of tacrine(4).

Another study, this one a randomized controlled trial, administered EGb 761 to 75 patients with early Alzheimer's disease at 120 mg per day and gave 75 Alzheimer's patients a placebo(6). This study lasted for one year. The patients that were given EGb 761 had significantly higher scores on two cognitive tests - the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAD-Cog) and the Geriatric Evaluation by Relative's Rating Instrument. The first test measures cognitive function and the second measures daily living and social behavior(6). This study would seem to suggest a possible benefit of ginkgo extract in early Alzheimer's and suggests further investigation.

Another, more scientific study looked into the mechanisms of ginkgo biloba extract on the cells of the brain. This study, conducted in 2001, involved administering EGb 761 to mice, then

looking at the genes that were affected by the herb(9). The study found that EGb 761 up-regulated several genes that neuroprotective roles. One of these was the gene that encodes transthyretin, which is a hormone that has been found in low levels in Alzheimer's disease patients(9). The ginkgo extract also enhanced the function of many other genes that are important in neural function. This would seem to contribute to the theory that Ginkgo enhances cognitive function.

One last study took a look at the individual components of EGb 761, namely the flavonoid component that makes up 24% of standardized Ginkgo Biloba(1). Many studies have shown that ginkgo biloba is a free radical scavenger. Free radicals are highly reactive oxygen species that can cause damage to unsaturated membrane phospholipids(5). The brain, being high in these unsaturated phospholipids, is especially susceptible to oxidative damage(5). This study found that the flavonoid component of ginkgo biloba scavenges free radicals; in this case, the free radical Nitric Oxide(1). This scavenging effect protected and rescued hippocampal neuronal cells, supporting the use of ginkgo extract in cerebral insufficiency(1). This protective effect may even suggest a use for ginkgo in prevention of neural damage as well as treatment.

Despite this evidence supporting the use of Ginkgo Biloba extract in treatment of early Alzheimer's and other dementias, there are differing opinions. In 1996, Dr. Russell G. Robertson conducted a literature review of ginkgo biloba, and stated that while he believed that there were no harmful effects of ginkgo use at low levels, there were also no beneficial effects(7).

Compared to many medicinal treatments, ginkgo biloba has few adverse side effects. It is a blood thinner, and should not be used with Coumadin or any other anti-clotting therapy(3). In less than four percent of individuals taking ginkgo biloba, side effects like restlessness, diarrhea, nausea, headache, dizziness, and heart palpitations were reported(3). Ginkgo biloba is also not

recommended for pregnant or lactating women, and individuals have reported severe allergic reactions from eating the fruit and seeds of the Ginkgo tree(3). There has also been concern about ginkgo biloba, along with other herbal treatments, contributing to infertility; however, in the treatment of Alzheimer's disease this would not be an issue of concern(8).

Ginkgo biloba is not a miracle drug, nor does it do anything above and beyond the treatments that are already prescribed for early Alzheimer's disease and dementia. It is also limited by only being of use in the early stage of Alzheimer's disease. Once patients have progressed beyond this stage, the herb has not been found to have any beneficial effect. Also, ginkgo biloba can only relieve symptoms of the disease; it can do nothing to reverse or halt the progression of the disease itself. Alzheimer's disease is incurable(5) and cannot be reversed by any known treatment. Besides that, not every ginkgo biloba on the market will provide the same effect. There are more than twenty-four different brands of ginkgo biloba sold in the United States(4). The only ones that will provide the effect produced in ginkgo biloba studies are the standardized extracts containing 24% flavonoids and 6% terpenoids. Lastly, the study of ginkgo biloba's effect on Alzheimer's disease is still in the early stages, and more testing is required to verify the benefit of ginkgo biloba treatment.

Conclusions

Alzheimer's disease is a progressive, debilitating dementia that robs it's victims of their memory, personality, and eventually, their life. In the investigations for treatment of this disease, ginkgo biloba has been shown preliminarily to have some beneficial effect in relieving early symptoms and prolonging progressive of the dementia for a short while. While further testing needs to be done before ginkgo can be approved for treatment, it has shown promise in alleviating the symptoms of early Alzheimer's disease.

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