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Green Tea Mouthwash and the Prevention of Porphyromonas Gingivalis: Reducing the Risk of Developing Alzheimer's Disease

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ABSTRACT

Alzheimer's disease causes 10% of all deaths in the United States, while severe periodontitis affects 10% of the population worldwide. Although seemingly unrelated, researchers exploring the connection between the two suggest that oral hygiene is necessary to decrease periodontitis that could possibly lead to Alzheimer's disease. A notable oral pathogen, *Porphyromonas gingivalis (P. gingivalis),* has been identified in the connection between Alzheimer's and periodontitis. In this study, green tea mouthwash is being analyzed to find out if the mouthwash can reduce the periodontitis mechanisms of *P. gingivalis* to reduce the risk of developing Alzheimer's. Green tea mouthwash contains the catechins, EGCg and ECg, which have been found to decrease Gram-negative and Gram-positive oral bacteria as well as proinflammatory cytokines such as IL-1β, IL-6, and TNF-α that *P. gingivalis* can induce orally and in the brain. In addition, *P. gingivalis* induces the formation of oral plaque, causing periodontitis, which green tea mouthwash has also been found to reduce. Compared to the traditional chlorhexidine mouthwash, green tea mouthwash causes little to no staining, may taste better, and can be used as drinking tea while having plaque-reducing abilities comparable to chlorhexidine. However, since Alzheimer's primarily affects the elderly, a proposal of green tea mouthwash being implemented in young adults aged 20 to 30 to proactively prevent Alzheimer's may be proposed since the risk of severe periodontitis and plaque, as well as amyloid beta (Aβ) concentration, increases with age and elevates at age 60. In addition, early-onset Alzheimer's has been found to occur at an average age of 56. However, the disease could affect those between the age of 30 and 40. Therefore, implementing green tea mouthwash into the dental care of young adults may prevent the risk of these individuals developing Alzheimer's prior to the age where the treatment may no longer be effective.

KEYWORDS

Alzheimer's Disease • Green Tea Mouthwash • Periodontitis • *Porphyromonas gingivalis* • Proinflammatory Cytokines • Oral Bacteria • Plaque Reduction

Introduction

The mortality rate of Alzheimer's, a neurodegenerative disease that mostly affects the elderly, has been increasing over time and is projected to increase in the next 20 to 30 years (Matthews et al., 2018; Ding et al., 2018; Wu et al., 2021). For Alzheimer's disease, the total direct medical expense in the United States is projected to increase from $236 billion in 2016 to more than $1 trillion in 2050, which does not take into consideration the indirect costs, which include caregivers (Deb et al., 2017). In 2015, unpaid caregivers for Alzheimer's disease provided around 18.1 billion hours of assistance, valued at about $221.3 billion. (Deb et al., 2017) According to Ding et al. (2018), Alzheimer's develops due to the build-up of beta amyloid (Aβ) within the brain. However, the cause of the Aβ buildup has not been identified, so there have not been any clear treatments developed to date (Wu et al., 2021).

There is a link between periodontitis and Alzheimer's due to the short distance from the oral cavity to the brain (Wu et al., 2021). According to Ding et al. (2018), periodontitis is the infection of the periodontium and is a chronic peripheral inflammatory disease initiated by oral microbes residing in the oral cavity. In particular, *Porphyromonas gingivalis* (*P. gingivalis*) has been associated with periodontitis (Charoensaensuk et al., 2021). *P. gingivalis* is a nonmotile oral pathogen that is common in periodontitis due to its fimbria, gingipains, and lipopolysaccharide (Ding et al., 2018). *P. gingivalis* can increase the risk of developing Alzheimer's by inducing plaque formation, oral inflammation, and neuroinflammation (Charoensaensuk et al., 2021; Ding et al., 2018; Furutama et al., 2020). Inflammation has been found to affect the blood-brain barrier, which is composed of blood vessels lined by endothelial cells that protect the brain from pathogens and toxins (Furutama et al., 2020). Furutama et al. (2020) noted that a damaged blood-brain barrier may result in cognitive impairment, brain damage, and neurodegenerative disorders.

To combat the mechanisms of *P. gingivalis*, oral hygiene such as toothbrushing, flossing, and mouthwash have been found to be effective methods, but mouthwash has been seen to have more reduction in plaque specifically (Luis et al., 2017; Bosma et al., 2022; Milleman et al., 2022, Caton et al., 1993). Because mouthwash has been found to reduce plaque, methods and ingredients targeted at reducing *P. gingivalis*, and ultimately Alzheimer's, are being studied.

P. gingivalis Induced Plaque Development and Survival in the Oral Cavity

Because *P. gingivalis* is a stationary pathogen, it adheres to host oral cells as well as to other oral bacteria such as *Streptococcus gordonii* (*S. gordonii*) and manipulates them for survival and colonization by creating oral plaque.

Lee et al. (2018) anaerobically cultured *P. gingivalis* and obtained human gingival epithelial cells from adult patients with tooth crown lengthening or impacted third molar extraction after oral surgery (p. 11). Lee et al. (2018) found that *P. gingivalis* invaded, replicated, and survived in human gingival epithelial cells, and that it could spread to other places (p. 2). Lee et al. (2018) stated that once *P. gingivalis* adheres to the host cells, it manipulates the cell's immune response to promote its own survival (p. 2).

Lee et al. (2018) observed that *P. gingivalis* trafficks into the vacuoles and the endoplasmic reticulum (ER) in the cells, which are important for maintaining cell homeostasis or autophagy (p. 6). Lee et al. (2018) reported that *P. gingivalis* spread from 60% to 80% from 3 to 24 hours of infection in the vacuoles (p. 3). In the endoplasmic reticulum, Lee et al. (2018) claimed that *P. gingivalis* colocalized in the ER at 100% after 6 hours and stayed constant even after 24 hours (p. 8). Lee et al. (2018) noted that by trafficking into these organelles, *P. gingivalis* induces autophagy, allowing it to avoid immune surveillance in the cell and survive (p. 8). When *P. gingivalis* travels into the vacuoles and reduces the size of the cytosol, the oral microbe takes away the cell's ability to store its own nutrients and to clean out the cell. Therefore, the cell has no way to regenerate and clean out the dead materials rendering it useless. Eventually, the cell may be unable to maintain homeostasis and may induce apoptosis. *P. gingivalis* may induce continuous apoptosis, destroying tissues and essential parts of both the oral and brain cavity which could cause systemic diseases such as Alzheimer's (Lee et al., 2018).

In a study of seven varied species of bacteria, Periasamy and Kolenbrander (2009) introduced the seven species in saliva coated glass and found that *P. gingivalis* had a specificity to grow with *S. gordonii* (p. 3). Periasamy and Kolenbrander (2009) claimed that *P. gingivalis* can adhere to saliva coated glass but cannot grow and build biofilms without adhering to other species such as *S. gordonii, A. oris, Veillonella sp.*, *F. nucleatum,* and *A. actinomycetemcomitans* colonizers but expressed specificity with initially colonizing streptococci (p. 6). Although Lee et al. (2018) observed that *P. gingivalis* adheres to gingival cells, the findings of Periasamy and Kolenbrander (2009) highlight this mechanism. *P. gingivalis* must adhere to some other primary colonizer or cells that allow it to survive. On its own, *P. gingivalis* cannot survive and may perish.

Periasamy and Kolenbrander (2009) inoculated *P. gingivalis, S. gordonii,* and *S. oralis* into separate flow cells and after 4 hours and 18 hours (p. 3). Periasamy and Kolenbrander (2009) found that at four hours, all the bacteria attached to the saliva surface with *P. gingivalis* at 1.00E047 μm^3, *S. gordonii* at 1.00E052 μm^3, and *S. oralis* at a little more than 1.00E043 μm^3 (p. 3). Periasamy and Kolenbrander (2009) reported that at eighteen hours, *P. gingivalis* was at 1.00E037 μm^3, *S. gordonii* was at the same μm^3, and *S. oralis* was at 1.00E41 μm^3 (p. 3). To see flow cells with two species, Periasamy and Kolenbrander (2009) paired each bacterium with *P. gingivalis* and recorded them at 4 and then again at 18 hours (p. 3). Periasamy and Kolenbrander (2009) reported that *P. gingivalis* with *S. oralis* had no growth or decrease from 4 and 18 hours (constant at 1.00E043 μm^3) and *P. gingivalis* with *S. gordonii* decreased from 1.00E037 μm^3 to 1.00E035 μm^3 between the hours (p. 3).

Periasamy and Kolenbrander (2009) stated that *P. gingivalis* can have growth with a suitable initial colonizer (*S. Gordonii)* even in the presence of an unfavorable initial colonizer (*S. Oralis)* (p. 4). Periasamy and Kolenbrander (2009) reported that *P. gingivalis* grows well with *S. gordonii* and *S. oralis,* indicating that *P. gingivalis* has a high specificity with streptococci which account for 60 to 90% of initial colonizers of enamel (p. 4). Periasamy and Kolenbrander (2009) noted that as *P. gingivalis* cannot form a productive partnership with *S. oralis*, it

indicates that *P. gingivalis* may be considered among other early-colonizing species that also coaggregated with initial colonizers (p. 5).

In a study in which Lamont et al. (2002) injected *P. gingivalis* and *S. gordonii* onto glass coverslips and analyzed their adherence using scintillation spectroscopy and nitrocellulose blot assay, Lamont et al. (2002) reported that *P. gingivalis* adheres to *Streptococcus gordonii*, a primary colonizing organism, to form plaque (p. 2). Lamont et al. (2002) noted how *P. gingivalis* is a secondary colonizer and therefore, could adhere to *S. gordonii* to start the formation of plaque through the adherence of *P. gingivalis*' proteins and *S. gordonii*'s proteins (p. 2). Lamont et al. (2002) reported that *P. gingivalis* adhered rapidly to *S. gordonii* and accumulated progressively over the four-hour period of about 60-80 um (p. 4). In addition, Lamont et al. (2002) added that *P. gingivalis* expressed specificity when adhering to form biofilms and only adhered to S. gordonii's SspB BAR domain, which is a specific protein (p. 7).

Both Periasamy and Kolenbrander (2009) and Lamont et al. (2002) expressed *P. gingivalis'* specificity towards *S. gordonii* when it comes to the formation of plaque and biofilms. *P. gingivalis* can adhere to *S. gordonii*, allowing *P. gingivalis* to manipulate *S. gordonii* to utilize its nutrients to survive in the oral cavity. *P. gingivalis*' survival is essential for it to travel into the brain through the bloodstream and adhere to brain endothelial cells, affecting the brain. Like the findings of Lee et al. (2018), *P. gingivalis* must adhere to some type of host cell or microbe to survive long enough to then travel to the brain.

In a study in which Wu et al. (2021) analyzed 17 elderly patients with Alzheimer's disease and 18 elderly patients without Alzheimer's for oral health, Wu et al. (2021) utilized the PacBio single molecule real-time (SMRT) to identify plaque as well as Linear discriminant analysis effect size (LEfSe) to analyze the diversity of bacteria and found that the Alzheimer's group had increased Lactobacillales, Streptococcaceae, Actinomycetales, and Veillonellae (p. 6). Wu et al. (2021) reported that the Alzheimer's group had 2.5% Lactobacillales, 5% Streptococcacea, 2% Actinomycetales, and 10% Veillonellae (p. 6). However, Wu et al. (2021) asserted that the diversity of bacteria in the Alzheimer's group was less than the control group with certain bacterium elevated (p.4). Wu et al. (2021) noted that the patients with Alzheimer's had 10 missing teeth while the control group had 5 missing teeth, and the Alzheimer's group had a dental plaque weight of 0.05 while the control had a dental plaque weight of 0.02 with a p-value less than 0.05 (p. 4). Wu et al. (2021) noted that the missing number of teeth and dental plaque weight was higher in the Alzheimer's group than the control (p. 4).

Periasamy & Kolenbrander (2009) claimed that *P. gingivalis* could grow with *Veillonella, F. nucleatum*, and *A. actinomycetemcomitans.* Since Actinomycetales and Veillonellales were more prevalent in the Alzheimer's group, *P. gingivalis* could adhere to these primary colonizing bacteria in the oral cavity and survive to travel to the brain through the bloodstream, causing neuroinflammation that leads to brain deficits. The colonization and adherence of *P. gingivalis* to other bacteria and cells is essential for it to colonize deeper within the body and to survive to produce enough damage to cause problems. In addition, Lamont et al. (2002) stated that *P. gingivalis* expressed specificity with *S. gordonii* and grew best with that bacterium. Since the group with

Alzheimer's had increased Veillonellae, Actinomycetales, and Streptococcacea, *P. gingivalis* may colonize with these primary colonizers, specifically Streptococcacea, and utilize these bacteria to emit more damage on the body. By adhering to these primary colonizers, *P. gingivalis* can utilize them for its own benefit such as for nutrients to survive or to build plaque biofilms. In addition, Wu et al. (2018) found that the Alzheimer's group had increased missing teeth and a higher dental plaque weight. Both oral defects are caused by periodontitis, which may be caused by *P. gingivalis*. The reason these bacteria may be prevalent in elderly with Alzheimer's may be due to *P. gingivalis*' influence through inflammation and periodontitis that may lead to neuroinflammation in the brain.

In contrast, Wu et al. (2021) stated that the control group had an elevated presence of Porphyromonadaceae while the Alzheimer's group did not (p. 6). Wu et al. (2021) reported that the members of Lactobacillales (2%), Streptococcaceae (5%), Actinomycetales (2.5%), and Veillonellales (10%) were prevalent in the Alzheimer's group while the control group had Fusobacteriaceae (5%), Cardiobacteriaceae (0.6%), and Porphyromonadaceae (5%) prevalent (p. 6). In addition, Wu et al. (2021) noted that the number of OTU (operational taxonomic units) and the level of diversity of bacteria in the Alzheimer's group was less than the control group (p. 4). In the Alzheimer's group, Porphyromonas was not elevated since *P. gingivalis* had adhered to the other prevalent bacteria, increasing their presence instead. Porphyromonas were elevated in the control group because the microbe was present in the mouth but had not been able to adhere to other host entities such as in the Alzheimer's group, which is also why Wu et al. (2021) found that the Alzheimer's group generally had worse oral health. These findings suggest that *P. gingivalis* has an inability to survive and colonize without the assistance of other host entities.

Evidence of Cognitive Impairment Due to *P. gingivalis*

Because *P. gingivalis* produces proinflammatory cytokines in the brain and adheres to endothelial cells, *P. gingivalis* can cause neuroinflammation that may lead to cognitive deficits and an increasing risk of developing Alzheimer's.

In a study in which Ding et al. (2018) orally injected 15 young and 15 middle-aged mice with *P. gingivalis,* left the rest to be the control, and then evaluated the mice on the Morris Water Maze, which is a test to assess spatial learning and memory, Ding et al. (2018) reported that *P. gingivalis* infection was found to cause cognitive decline and memory deficits in middle aged mice (p. 3). Ding et al. (2018) analyzed the mice over a four-day period on how long it took them to reach the platform in the maze to indicate if the mice remembered where it was (p. 3).

Ding et al. (2018) reported that young mice with *P. gingivalis* infection as well as mice from both control groups had decreasing Morris Water Maze times over the four days from 40 seconds to 22 seconds, while the middle-aged mice with *P. gingivalis* infection had times staying constant over the four days at 40 seconds with a $p < 0.05$ (p. 3). Ding et al. (2018) noted that both young mice groups decreased in their times from 50 to about 35 seconds (p. 3). Ding et al. (2018) also noted that the middle-aged mice with *P.*

gingivalis crossed over the platform 10 times while the control middle-aged group only crossed it 5 times, which was noted towards their spatial awareness being decreased after infection with a $p < 0.05$ (p. 3). Ding et al. (2018) noted that both young mice groups crossed the platform 5 times (p. 3). Ding et al. (2018) concluded that *P. gingivalis* infection in middle-aged mice impaired spatial learning and memory abilities (p. 3).

In addition, Ding et al. (2018) noted that the concentration of TNF-α, IL-6, and IL-1β was increased in the brains of middle-aged mice with *P. gingivalis* (p. 4). Ding et al. (2018) noted that the concentration of TNF-α in *P. gingivalis* middle-aged mice was 125 pg/mL but in control middle-aged mice, it was 50 pg/mL (p. 4). Ding et al. (2018) stated that the concentration of IL-6 was 8 pg/mL in *P. gingivalis* middle-aged mice while 40 pg/mL in the control middle-aged mice. Ding et al. (2018) reported that the concentration of IL-1β was 40 pg/mL in the *P. gingivalis* middle-aged mice and the concentration was 20 pg/mL in the control middle-aged mice. Ding et al. (2018) noted that for all proinflammatory cytokines, the young mice groups expressed the same amount which was 40 pg/mL (p. 4). Ding et al. (2018) concluded that, "*P. gingivalis* infection may promote neuroinflammation by increasing the expression of the pro-inflammatory cytokines TNF-α, IL-6, and IL-1β in the brain tissues of middle-aged mice" (p.4). The increased production of proinflammatory cytokines in the *P. gingivalis* infected mice may indicate that elevated inflammatory response can result in brain damage because of neuroinflammation.

In a study in which Charoensaensuk et al. (2021) injected six-to-seven-week-old mice brains with live *P. gingivalis* and then compared the brains to control mice brains with heat-killed *P. gingivalis* by observing cell apoptosis and proinflammatory cytokine numbers, Charoensaensuk et al. (2021) found that *P. gingivalis* adhered to brain endothelial cells and the adherence induces the upregulation of the NF-kB pathway which led to the induction of proinflammatory cytokines, IL-1β and TNF-α, which caused inflammation and apoptosis (p. 16). Charoensaensuk et al. (2021) noted that the blood-brain barrier that protects homeostasis of the central nervous system is made up of brain endothelial cells (p. 2). Charoensaensuk et al. (2021) added that the brain endothelial cells maintain the structure of the blood-brain barrier and destruction such as inflammation to the barrier leads to issues within the brain (p. 2).

Charoensaensuk et al. (2021) reported that the cell survival rate decreased due to *P. gingivalis* infection from 30% to 70% and there was no difference by the heat-killed bacteria (p. 9). Charoensaensuk et al. (2021) concluded that the infection with live *P. gingivalis* induced and effected cell death in brain endothelial cells while heat-killed did not (p. 9). In addition, Charoensaensuk et al. (2021) reported that only live *P. gingivalis* can infect brain endothelial cells and induce proinflammatory cytokine expression as live bacteria increased the IL-1β protein as well as TNF-α protein expression (p. 11). Charoensaensuk et al. (2021) reported that IL-1β expression increased from a level of 0 to 2 while the expression of TNF-α increased from a level of 0 to about 3 (p.11). Charoensaensuk et al. (2021) noted that *P. gingivalis* infection increases ROS production and NF- kB activation in brain endothelial cells as it enhanced ROS production and the NF-kB protein to the nucleus after exposure,

which can be seen as the expression increased from a level of 0 to 200 (p. 11). Charoensaensuk et al. (2021) stated that *P. gingivalis* infection induces brain endothelial cell apoptosis and cell death through the expression of ROS/ NF-kB/ proinflammatory cytokines as NAC, a ROS production neutralized and cell death protector, was able to reduce ROS production in *P. gingivalis* cells and nuclear translocation of NF-kB; both after the *P. gingivalis* infection (p. 12).

In a study in which Furutama et al. (2020) injected mice with periodontal disease, excised their brains, then analyzed the brains for proinflammatory cytokine levels after one week, Furutama et al. (2020) reported that the level of proinflammatory cytokines was increased in the mice (p. 8). Furutama et al. (2020) reported that the level of TNF-α did not change, increasing from 1 to 2 Pg/mL while both levels of IL-6 and IL-1β increased; 0 to 100 Pg/mL for IL-6 and 2 to 6 Pg/mL for IL-1β (p. 8). Furutama et al. (2020) noted that the elevated levels decreased until 8 weeks with a p-value less than 0.05 (p. 8). In addition, Furutama et al. (2020) injected the mice with an immunofluorescent to analyze for periodontal disease or 3-kDa dextran levels that infiltrated the blood-brain barrier and into the hippocampus after one week (p. 9). Furutama et al. (2020) reported that the dextran levels in mice with periodontal disease was 3 compared to the control that had a dextran level of 1 with a p-value less than 0.01 (p. 9). Furutama et al. (2020) reported that periodontal inflammation induced IL-1β expression in the hippocampus that was dependent on increases in serum IL-6 levels, which overall increased BBB permeability (p. 9).

By adhering to host brain cells, *P. gingivalis* can induce the expression of proinflammatory cytokines that can result in excessive inflammation. Inflammation can result in a large amount of healthy cells dying due to the damage, resulting in neurodegeneration. The study done by Furutama et al. (2020) supports the findings of Charoensaensuk et al. (2021) and Ding et al. (2018) as *P. gingivalis* was found to increase the production of proinflammatory cytokines in the brains of mice. However, Furutama et al. (2020) reported that the expression of TNF-α in the brains did not increase while Charoensaensuk et al. (2021) and Ding et al. (2018) reported that TNF- α levels increased. However, the increased expression of the other proinflammatory cytokines, IL-1β and IL-6, still affirms the mechanism of *P. gingivalis* inducing the expression of those cytokines. Even if TNF-α is not found to be expressed or not found to be expressed as much, the other cytokines are still found to be induced by *P. gingivalis* within the brain and can cause damage such as cognitive deficits especially if the damage is done to the hippocampus.

Reduction of Plaque Using Mouthwash

Because plaque can be reduced through oral hygiene, mouthwash may be the best anti-plaque treatment as other treatments, such as tooth brushing and flossing, may not be as effective when it comes to reducing plaque.

In a study in which Luis et al. (2017) assigned 30 of 60 third-year dental students to use a Listerine Cool Mint mouthwash and assigned the other 30 to use dental floss for two weeks, Luis et al. (2017) claimed that essential oil mouthwash is more effective than dental floss at reducing dental plaque (p. 1). Luis et al. (2017) reported that on the plaque

index after the two weeks, the mouthwash group reduced by 29.5% while the dental floss only reduced 18% with a p-value less than 0.001 (p. 3). Luis et al. (2017) reported that the mouthwash group reduced interproximal plaque index by 36.5% while the dental floss group reduced interproximal plaque index by 17.5% (p. 3). Although oral hygiene techniques, such as flossing, can be used to decrease plaque production, mouthwash may be the most effective method. Traditional mouthwash for plaque reduction uses chlorhexidine as the main ingredient. However, other ingredients may be explored to efficiently target *P. gingivalis* and its mechanisms.

In a study in which Bosma et al. (2022) assigned healthy adult participants to either use a hydro alcohol rinse, mouthwash, professional flossing, or self-flossing for twelve weeks, Bosma et al. (2022) claimed that the mouthwash improved all outcome measures when compared to the other treatments (p. 1). Bosma et al. (2022) reported that on the plaque index compared to the hydro alcohol, the mouthwash reduced 22.8%, the professional flossing reduced 5%, and the supervised flossing reduced 2.4% after twelve weeks (p. 7). Bosma et al. (2022) reported that the interproximal mean plaque index, at weeks 4 and 12, was reduced for the mouthwash group by 29.5% at week 4 and 22.8% at week 12, for the professional flossing group by 11.7% at week 4 and 5.0% at week 12, and for the flossing under supervision group by 6.7% at week 4 and 2.4 on week 12 (p. 5).

In a study in which Milleman et al. (2022) divided volunteers into four groups: toothbrushing only, toothbrushing and mouth rinsing, toothbrushing and flossing, and toothbrushing, flossing, and mouth rinsing and analyzed the volunteers for plaque accumulation after twelve weeks, Milleman et al. (2022) claimed that the oral treatments that included the use of a mouth rinse reduced plaque (p. 1). Milleman et al. (2022) noted that the participants were provided with appropriate dental training and performed their regimen at home, under virtual supervision, once each day, and then the second daily use and weekends were unsupervised (p. 1). Milleman et al. (2022) reported that the toothbrushing and mouth rinsing groups reduced plaque by 35.8% and the toothbrushing/rinsing/flossing group reduced plaque by 32.8% when compared to the toothbrushing only and toothbrushing and flossing groups with a p-value of less than 0.001 (p. 7). Milleman et al. (2022) noted that interproximal plaque was reduced by the toothbrushing and rinsing group by 30.3% and the toothbrushing/rinsing/flossing group by 28.4% compared to the toothbrushing only group that reduced it by 26.9% and the toothbrushing and flossing group which reduced it by 24.9% with a p-value less than 0.001 (p. 7). Similar to Luis et al. (2017) and Bosma et al. (2022), Milleman et al. (2022) also suggested that mouthwash may be the most effective method for plaque reduction. Although, in the study done by Milleman et al. (2022), mouthwash was used in addition to flossing or toothbrushing, the claim that mouthwash may be the most effective method for plaque is still suggested since normal oral hygiene, such as toothbrushing and flossing, is already a part of the daily oral routine for many individuals. Mouthwash is not a normal daily procedure for many; therefore, this suggests that the addition of mouthwash to an individual's oral hygiene routine may be effective for plaque reduction.

In a study in which Caton et al. (1993) assigned 92 healthy male subjects aged 18 to 28 to either chlorhexidine mouthwash and toothbrushing, interdental cleaners and toothbrushing or to their existing oral hygiene regimen to analyze plaque reduction, Caton et al. (1993) claimed that only interdental plaque removal combined with toothbrushing is effective in reducing interdental inflammation (p. 2). Caton et al. (1993) reported that after three months, the existing regimen groups reduced mean bleeding from 47.50% to 40.46%, the mouthwash group reduced mean bleeding from 54.65% to 47.08%, and the interdental group reduced mean bleeding from 56.09% to 5.70% (p. 4). Caton et al. (1993) stated that bleeding after stimulation indicated that there was a presence of inflammation in gingival tissue (p. 1). Therefore, Caton et al. (1993) affirmed that only the interdental cleaner with toothbrushing was sufficient at reducing bleeding scores due to inflammation (p. 4).

Plaque can cause bleeding within the mouth as it damages the gums, making them irritated and inflamed. Caton et al. (1993) expressed that only interdental cleaners with toothbrushing can reduce the bleeding due to plaque when compared to mouthwash, contradicting the findings of Luis et al. (2017), Bosma et al. (2022), and Milleman et al. (2022). However, the bleeding occurs after the plaque has had time to settle within the mouth and gums. The use of mouthwash prior to plaque settling may be more effective as suggested by the findings of Luis et al. (2017), Bosma et al. (2022), and Milleman et al. (2022). The interdental cleaners with toothbrushing may be effective after the plaque has settled, however, using mouthwash to reduce the plaque before the plaque has had time to colonize in the oral cavity may be more beneficial for individuals.

Reduction of *P. gingivalis* and Alzheimer's Using Green Tea Mouthwash

Because green tea mouthwash catechins can decrease oral bacteria and proinflammatory cytokines, green tea mouthwash may be used as an anti-plaque treatment that could decrease neuroinflammation and the risk of Alzheimer's.

In a study in which Kaur et al. (2014) assigned 15 of 30 participants from the ages of 18 to 25 years old to a green tea mouthwash and 15 of them to a chlorhexidine mouthwash, Kaur et al. (2014) reported that the difference between the plaque score of the two mouthwashes was not statistically significant with p-values greater than 0.05, indicating that the mouthwashes had similar plaque reduction (p. 10). Specifically, Kaur et al. (2014) found that the green tea catechins, EGCg and ECg, had similar plaque reduction when compared to the traditional chlorhexidine mouthwash (p. 10). In addition, Kaur et al. (2014) reported that the green tea had a mean plaque score of 2.763 while the chlorhexidine had a mean plaque score of 2.1900 with a p-value greater than 0.05, indicating that there was no difference between the two mouthwashes (p. 19). Kaur et al. (2014) also noted that EGCg and ECg decreased gram-positive and gram-negative bacteria in the oral cavity (p. 5). Chlorhexidine mouthwash is traditionally prescribed due to its notable plaque reduction. However, to decrease the risk of developing Alzheimer's and plaque, green tea mouthwash may be a comparable prospect due to its catechins. In addition to

green tea's plaque reduction when compared to chlorhexidine, the catechins can decrease gram-positive and gram-negative bacteria. Considering that *P. gingivalis* and *S. gordonii* are two notable pathogens when it comes to periodontitis-induced Alzheimer's and are gram-negative and gram-positive, green tea mouthwash can be used to decrease pathogenesis in the oral cavity. A lack of *P. gingivalis* and *S. gordonii* in the oral cavity may reduce plaque biofilm formation, and overall the risk of developing Alzheimer's disease.

In a study in which Sarin et al. (2015) assigned 110 workers aged 18 to 60 years old to either a placebo mouthwash or to a green tea mouthwash for 28 days, Sarin et al. (2015) reported that green tea mouthwash decreased the plaque index scores from 3.43 to 1.77 with a p-value less than 0.05 (p. 5). Sarin et al. (2015) added that the green tea mouthwash was made from an extract of leaves of *Camellia sinensis* (p. 2). Sarin et al. (2015) suggested that green tea mouthwash produces a similar reduction in plaque when compared to the traditional chlorhexidine mouthwash. Since plaque is an important colonization mechanism of *P. gingivalis,* green tea mouthwash reducing plaque can in turn reduce the presence of *P. gingivalis* and eliminate the oral microbe's ability to survive in the oral cavity.

In a study in which Cai et al. (2015) orally injected eight-week-old female mice with *P. gingivalis*, gave the mice EGCg through water, and then sacrificed the mice after seven weeks, Cai et al. (2015) found that EGCg decreased IL-1β, IL-6, and TNF-α production (p. 3). Cai et al. (2015) reported that although *P. gingivalis* increased the production of IL-1β, IL-6, and TNF-α, initially the introduction of catechin EGCg decreased the production of the cytokines (p. 3). Cai et al. (2015) reported that EGCg decreased the levels of IL-1β from 976 pg/mL to 531 pg/mL with a p-value less than 0.01 (p. 4). Cai et al. (2014) noted that IL-6 decreased with EGCg with a p-value less than 0.05, but TNF-α decreased without being statistically significant with a p-value greater 0.05 (p. 3). Like the study done by Kaur et al. (2014), green tea catechin, EGCg, was found to reduce a mechanism of *P. gingivalis* in the findings of Cai et al. (2015). Reducing the proinflammatory cytokines that *P. gingivalis* induces can decrease inflammation in the oral cavity and can halt *P. gingivalis* from being able to travel into the brain to induce neuroinflammation. If *P. gingivalis* is unable to colonize in the oral cavity by inducing proinflammatory cytokines, the microbe may be unable to survive in the mouth before it can travel to the brain.

In a study in which Cho et al. (2013) treated 48 rats with EGCg or a saline control after periodontitis was induced and analyzed the rats for inhibited cytokine expression, Cho et al. (2013) claimed that administration of EGCg can inhibit cytokine expression and therefore, can have a therapeutic effect on damaged periodontal tissue (p. 1). Cho et al. (2013) reported that the number of TNF-α positive cells in connective tissue decreased from 100 to 75 cells with EGCg and increased with the control from 150 to 250 cells with a p-value less than 0.05 (p. 5). Cho et al. (2013) stated that the number of TNF-α positive cells in alveolar bone decreased from 150 to 100 cells with EGCg but increased with the control from 200 to 300 cells with a p-value less than 0.05 (p. 5). Cho et al. (2013) reported that the number of IL-6 positive cells in connective tissue stayed constant with EGCg at 200 but decreased with the control from 600 to 500 cells (p. 5). Cho et al. (2013) stated

that the number of IL-6 positive cells in alveolar bone decreased with EGCg from 500 to 400 cells and increased from 600 to 900 cells then decreased to 600 cells with the control (p. 5). Cho et al. (2013) claimed that when EGCg is administered orally, it can decrease proinflammatory cytokines such as TNF-α and IL-6 in periodontitis (p. 7).

Both Cho et al. (2013) and Cai et al. (2014) expressed EGCg's ability to reduce the production of proinflammatory cytokines. The reduced cytokines are essential to inhibiting *P. gingivalis'* ability to not only colonize but to cause severe periodontitis and plaque within the oral cavity. When *P. gingivalis* causes severe periodontitis and plaque, it allows *P. gingivalis* to survive in the mouth long enough to travel through the bloodstream and then into the brain where it may adhere to the blood-brain barrier and induce cytokines. The inflammation in the brain may then lead to the possibility of systemic diseases such as Alzheimer's occurring as inflammation can affect the connections within the brain. However, with the introduction of green tea mouthwash into the daily dental routine, *P. gingivalis* may be unable to carry out these mechanisms as Sarin et al. (2015) and Kaur et al. (2014) found that green tea mouthwash can reduce plaque formation and *P. gingivalis* levels, while Cho et al. (2013) and Cai et al. (2014) reported that green tea mouthwash may reduce the proinflammatory mechanism of *P. gingivalis.* Therefore, *P. gingivalis* may be rendered useless and may die before the microbe could get the chance to harm the brain.

Comparison of Green Tea Mouthwash and Chlorhexidine Mouthwash

Because green tea mouthwash has similar plaque reduction as the traditional chlorhexidine mouthwash, it may be used instead of chlorhexidine as green tea tastes better to some, and has reduced staining capabilities, which may be preferable on top of its ability to decrease the risk of Alzheimer's.

In a study in which Priya et al. (2015) assigned 30 patients to either a chlorhexidine or green tea mouthwash for the course of a month, Priya et al. (2015) reported that green tea mouthwash showed more reduction in bleeding in the mouth with a decrease from 82.71 to 32.01 on the bleeding index compared to chlorhexidine mouthwash which had a decrease from 82.5 to 46.01 on that same index with a p-value less than 0.05 (p. 14). Priya et al. (2015) concluded that green tea induced a decrease in oral bacteria and reduced inflammation which could have caused the decrease in the bleeding index (p. 20). Priya et al. (2015) found that there were no differences in staining of the teeth or the tongue between the chlorhexidine and green tea groups (p. 4). Priya et al. (2015) reported that the tooth stain with chlorhexidine was 0.25 on the tooth stain index while the tooth stain with green tea was 0.26 on the tooth stain index (p. 7). On the same index, Priya et al. (2015) stated that the tongue stain with chlorhexidine was 0.20 while with green tea, the tongue stain was 0.22 (p. 7).

Plaque in the mouth that is caused by *P. gingivalis* can be severe enough to cause bleeding due to damage in the mouth. However, Priya et al. (2015) suggested that green tea mouthwash can decrease more bleeding in the mouth when compared to chlorhexidine mouthwash, which indicates that green

tea mouthwash may be a better method to decrease periodontitis or the effects of periodontitis. As a result, green tea mouthwash may be seen as an alternative method to decrease the risk of Alzheimer's as it may have similar if not better mechanisms than the traditional chlorhexidine mouthwash.

In a study in which Parwani et al. (2013) assigned 90 students over the course of 4 days to either a chlorhexidine mouthwash or an herbal mouthwash and gave the students a questionnaire at the end of the study, Parwani et al. (2013) found that those who used chlorhexidine mouthwash instead of the herbal mouthwash had staining as well as a mild alteration in taste for salty foods and drinks (p. 22). Parwani et al. (2013) reported that 19 subjects in the chlorhexidine group reported staining and 16 subjects in the chlorhexidine groups reported a mild alteration in taste for salty foods while 1 subject in the green tea group reported alteration in taste and no subjects reported staining in the green tea group (p. 24). Parwani et al. (2013) concluded that herbal mouthwash has a lesser tendency for side effects such as staining (p. 26).

Priya et al. (2015) noted that the staining between chlorhexidine mouthwash and green tea mouthwash had similar numbers. However, Parwani et al. (2013) reported that chlorhexidine had more staining and altered the individuals' taste when compared to green tea mouthwash. Although the claim centering staining is contradictory, Parwani et al. (2013) found that chlorhexidine mouthwash alters one's taste. The staining, whether it comes from chlorhexidine or green tea mouthwash, can be managed and may not harm the mouth. However, the taste alteration could be more severe than expected and therefore, could permanently damage one's mouth. Therefore, even if green tea mouthwash does stain the mouth, it has not been found to affect an individual's taste and can reduce the damage that could lead to Alzheimer's, which may exceed the staining side effect.

In a study in which Eshghpour et al. (2013) assigned 44 patients in need of bilateral impacted third molar surgery between the ages of 18 to 30 to a green tea mouthwash or a placebo of distilled water after surgery and told the patients to rinse twice a day, Eshghpour et al. (2013) reported that those who used green tea mouthwash after mouth surgery used less pain medication when compared to distilled water with a p-value less than 0.05 (p. 16). Eshghpour et al. (2013) noted that the pain was self-reported pain based on the VAS assessment and the patients were asked to record the number of pain medications they took after surgery to be analyzed (p. 13). Eshghpour et al. (2013) reported that the mean pain level on the VAS was lower in the green tea mouthwash group with a decrease from 57.26 to 4.03 while the distilled water group had a mean decrease from 56.65 to 9.69 with a p-value of 0.001 (p. 17). Eshghpour et al. (2013) also reported that green tea is commonly available in eastern countries and its accessibility and cost make it more appropriate in some countries (p. 22). Eshghpour et al. (2013) asserted that rinsing with green tea may be beneficial to control complications after oral surgery including pain and can reduce the need for antibiotics or chlorhexidine mouthwash (p. 26).

In addition to green tea's ability to decrease bleeding, potentially staining, and reduce taste alteration when compared to chlorhexidine mouthwash, Eshghpour et al. (2013) reported that mouthwash can decrease pain after oral

surgery. If green tea mouthwash is implemented into the dental care of individuals, it may reduce the amount of pain individuals feel even if they do not have surgery, especially if they have sensitive mouths or cavities. The mechanisms and benefits that green tea mouthwash provides may indicate that utilizing green tea mouthwash instead of the traditional chlorhexidine mouthwash has other benefits in addition to reducing plaque and the other mechanisms of *P. gingivalis.*

Drinking Green Tea as a Method of Reducing the Risk of Alzheimer's Disease

Because green tea mouthwash may have benefits to cognitive deficits and can be used to reduce the risk of Alzheimer's disease, green tea alone as a drink may also be used as another simpler solution to reduce the risk of Alzheimer's.

In a study in which Shirai et al. (2019) randomly selected participants aged 40 to 79 years old from the NILS-LSA surveys in Japan and analyzed the participants to see if green tea or coffee could reduce the risk of cognitive decline in older adults, Shirai et al. (2019) reported that the intake of green tea was shown to reduce the risk of cognitive decline (p. 1). Shirai et al. (2019) reported that the surveys were conducted between 1997 to 2000 and were conducted every 2 years, up to seven times (p.2).

Shirai et al. (2019) reported that those with less than once a day intake of green tea had a 39.7% incident of cognitive decline, once a day intake had a 28.8% incident, 2 to 3 times a day had a 32.7% incident, and more than 4 times a day had a 32.6% incident (p. 4). Shirai et al. (2019) claimed that the elevated intake of green tea daily resulted in a lower percentage of cognitive decline incidence (p. 4). In contrast, Shirai et al. (2019) stated that coffee intake had no notable association with reduced or increased cognitive decline incident (p. 4).

Drinking green tea frequently, such as multiple times a day, may be an alternative method to receive the catechins that green tea mouthwash contains which may reduce *P. gingivalis* and overall, Alzheimer's disease. Both the tea and the mouthwash come from the same leaf and may also be consumed orally as a drink and can have the same cognitive benefits that reduce the risk of Alzheimer's and the development of *P. gingivalis.*

In a study in which Ma et al. (2020) analyzed the cerebrospinal fluid (CSF) and frequency of green tea consumption in 722 cognitively intact participants from the Chinese Alzheimer's Biomarker and CABLE database, Ma et al. (2020) reported that those who had frequent consumption of green tea had lower volume levels of CSF (p. 4). Ma et al. (2020) noted that the CSF biomarkers of Alzheimer's were analyzed in the study, including the concentration of Aβ and linear models of the data were created based on the concentrations (p.4). Ma et al. (2020) reported that in all participants the level of CSF t-tau was -0.00428 with a p-value of 0.041. Participants aged less than 65 had a level of CSF t-tau of -0.00236 with a p-value of 0.491, and participants aged greater than 65 had a level of CSF t-tau of -0.00744 with a p-value of 0.007 (p. 5). Ma et al. (2020) found that in all participants the level of CSF t-tau/ Aβ42 was -0.05559 with a p-value of 0.088. Participants aged less than 65 had a level of CSF t-tau of -0.05324 with a p-value of 0.346, and

participants aged greater than 65 had a level of CSF t-tau of -0.08232 with a p-value of 0.039 (p. 5). Ma et al. (2020) reported that the value of CSF t-tau was statistically significant in all participants and those aged 65 and over, and the value of CSF t-tau/ Aβ42 was significant in participants aged 65 or older (p. 5).

Green tea mouthwash is made from the same base ingredient as the green tea beverage, and the ingredient is *Camellia sinensis.* Therefore, green tea itself being consumed could potentially be utilized as a method to decrease the risk of Alzheimer's. The findings of Ma et al. (2020) and Shirai et al. (2019) suggest this potential solution. Ma et al. (2020) found that the consumption of green tea in older individuals reduced the biomarkers of Alzheimer's disease that include Aβ concentration, which is the main cause of the disease itself. Green tea as a drink is made straight from the leaves of *Camellia sinensis,* although the green tea mouthwash is often created from the same leaves and is often mixed with the same percentage of chlorhexidine or other ingredients, such as baking soda. However, because both the tea and the mouthwash come from the same plant, they may be found to have cognitive benefits as the leaves of green tea contain the catechins that have been found to reduce oral bacteria, proinflammatory cytokines, and overall, the risk of Alzheimer's.

In a study in which Schimidt et al. (2017) supplemented two-month-old male Wistar rats with green, red, or black tea for eight weeks, injected some of the rats with Aβ intra-hippocampal infection and then analyzed the rats for memory deficits, Schimidt et al. (2017) reported that rats supplemented with green tea showed a decrease in damage in the brain (p. 4). Schmidt et al. (2017) added that the mice were subjected to memory tests (p. 3). Schimidt et al. (2017) noted that green tea was made from *Camellia sinensis* leaves and had concentrations of EGCg and ECg (p. 1).

Schimidt et al. (2017) reported that for the object recognition test, the Alzheimer's disease-like group had a value of discrimination index of 2.87 with a p-value of 0.001, the green tea decreased short-term memory with a value of 2.99 and a p-value of 0.009, red tea also decreased short-term memory with a value of 2.54 and a p-value of 0.02, and black tea had a value of 0.31 with a p-value of 0.75, where a high discrimination index or value indicates an increased ability to identify objects using short or long-term memory (p. 4). Schimidt et al. (2017) found that for the object recognition test, the Alzheimer's disease-like group had a discrimination index of 3.63 with a p-value of 0.002, the green tea decreased long-term memory deficits with a value of 4.97 and a p-value of 0.0001, red tea also decreased long-term memory deficits with a value of 4.23 and a p-value of 0.001, and black tea decreased long-term memory deficits with a value of 2.12 with a p-value of 0.04 (p. 4).

Similarly, to the findings of Ma et al. (2020) and Shirai et al. (2019), Schimidt et al. (2017) also found that green tea avoids or decreases long and short-term memory deficits, which is another symptom or biomarker of Alzheimer's. Schimidt et al. (2017) also added that the green tea was made from *Camellia sinensis* leaves and had high concentrations of EGCg and ECg, which are key catechins in the green tea mouthwash. In green tea mouthwash, the catechins decrease the risk of developing Alzheimer's by reducing oral bacteria such as *P. gingivalis*, plaque, and proinflammatory cytokines. Therefore, green tea, as a drink, may be used alternatively for people who may not want

to implement green tea mouthwash into their dental care but prefer to reduce the risk of developing Alzheimer's. However, Schimidt et al. (2017) also claimed that red tea avoided short and long-term memory deficits and black tea also avoided long-term memory deficits. Although this does affirm that these three teas can all benefit one's memory in some way, there are no current mouthwashes that are based off these teas specifically. In addition, red tea is created from a plant that does not have the same catechin properties as green tea. However, black tea is also made from the same leaves as green tea but was not found to avoid short-term memory deficits while green tea avoids both. This may be due to the other ingredients black tea may contain; however, this suggests that green tea may be consumed as a drink and still hold the same Alzheimer's prevention properties as green tea mouthwash.

The Proactive Implementation of Green Tea Mouthwash

Because Alzheimer's affects mostly elderly and treatment at that age is often too late and is not as effective, green tea mouthwash may be implemented into the practice of twenty- to thirty-year-old individuals as they are not at elevated risk for plaque development and cognitive decline to proactively prevent the risk of Alzheimer's development.

In a study in which Davidovich et al. (2020) obtained patient records of 1000 healthy children aged 2.5 to 7 years that visited a pediatric clinic and analyzed the records for characteristics that affect plaque accumulation, Davidovich et al. (2020) reported that the children were analyzed using the Modified Turesky Plaque index and claimed that as age increased, the risk of developing plaque increased (p. 1). Davidovich et al. (2020) reported that age contributed to plaque severity, with a 3% increase in the risk of developing moderate or severe plaque for every one month increase in age (p. 3).

Due to green tea's ability to decrease the risk of developing Alzheimer's, green tea mouthwash may be implemented into the dental hygiene routine of young adults aged twenty to thirty years old. Davidovich et al. (2020) reported that as age increases the risk of developing plaque increased. Therefore, as one reaches age twenty or age thirty, the risk of developing plaque is higher than if one was age ten. In addition, when individuals are younger, they do not develop plaque as much which can be seen as Davidovich et al. (2020) utilized two and a half years old to seven-year-old. Implementing the green tea mouthwash into the dental care of individuals that young may not have an effect as there is not much plaque development, however, young adults aged twenty to thirty are developing plaque especially biofilms developed due to *P. gingivalis*, which can become severe. Therefore, green tea mouthwash may be utilized to manage it before it becomes too severe and hard to contain as individuals grow older.

In a study in which 350 individuals aged 20 to 89 years old completed four 2-hour visits for cognitive testing, an MRI, and a PET scan for Aβ concentration. Rodrigue et al. (2012) found that Aβ concentration increased with age and was connected to cognitive deficits (p. 1). Rodrigue et al. (2012) noted that the two cognitive tests were the WAIS and the CANTAB for processing speed, working memory, episodic memory, crystallized abilities, and fluid reasoning (p. 3).

Rodrigue et al. (2012) reported that there was a linear increase in amyloid

with age with a p-value less than 0.001 (p. 4). In addition, Rodrigue et al. (2012) noted that individuals over the age of 60 had an increased concentration of Aβ (p. 4). Additionally, Rodrigue et al. (2012) ran tests for elevated Aβ in relation to cognitive deficits. Rodrigue et al. (2012) reported that there was a relationship between increasing Aβ and decreasing cognitive performance. Rodrigue et al. (2012) noted that there was a correlation with r= -0.55 and a p-value less than 0.02 for processing speed, r= -0.46 and a p-value equal to 0.05 for working memory, and r= -0.59 and a p-value equal to 0.01 for reasoning ability (p. 4). However, Rodrigue et al. (2012) stated that there was no association between Aβ and episodic memory or crystallized intelligence (p. 4).

Adjacent to Davidovich et al. (2020), Rodrigue et al. (2012) reported that the concentration of Aβ increased with age. Both Davidovich et al. (2020) and Rodrigue et al. (2012) reported that the two main contributors of periodontitis and Alzheimer's increase with age. Rodrigue et al. (2012) also reported that the concentration of Aβ rapidly increases at age sixty and is associated with decreased cognitive performance. Therefore, if green tea mouthwash is implemented into the dental care of adults aged twenty to thirty, the mouthwash may proactively work to prevent the buildup of plaque which may in turn, prevent the buildup of Aβ. The prevention of Aβ buildup may decrease the risk of developing Alzheimer's as the brain does not develop the Aβ buildup. When individuals are between the ages of 20 to 30, they are not at elevated risk for Aβ concentration and plaque buildup, so if the mouthwash is implemented then, it may be able to work efficiently for those individuals in the future.

In a study in which Holde et al. (2017) collected periodontal conditions from individuals aged 20 to 79 years old in Northern Norway, Holde et al. (2017) claimed that periodontitis prevalence and severity increased with age (p. 1). Holde et al. (2017) reported that in individuals aged 20 to 34, the percentage of severe periodontitis was 0.2%; in individuals aged 35 to 44, the percentage was 1.6%; in individuals aged 45 to 54, the percentage was 7.4%; in individuals aged 55 to 64, the percentage was 18%; and in individuals 65 to 79, the percentage was 23.7% (p. 5). However, Holde et al. (2017) reported that in individuals aged 20 to 34, the percentage of non-severe periodontitis was 15.8%; in individuals aged 35 to 44, the percentage was 33%; in individuals aged 45 to 54, the percentage was 46.4%; in individuals aged 55 to 64, the percentage was 57.9%; and in individuals 65 to 79, the percentage was 57.7% (p. 5). Holde et al. (2017) cited Novak et al. (2002) and claimed that severity and extent of periodontitis is expected as periodontitis is a chronic disease and is cumulative with time (p. 8).

In addition to the findings of Davidovich et al. (2020) and Rodrigue et al. (2021), Holde et al. (2017) reported that the severity and extent of periodontitis is cumulative with time. Davidovich et al. (2020) found that plaque development increases with time, which plaque is the main contributor to periodontitis. Therefore, as an individual increases in age, they develop more plaque, which can lead to severe periodontitis. However, if green tea mouthwash is utilized before the individual reaches an age where severe periodontitis is more likely, then the individual can decrease the risk of achieving the severe periodontitis and as a

result, can decrease their risk of developing Alzheimer's.

In a study in which Koedam et al. (2009) analyzed 297 patients with early-onset Alzheimer's before the age of 65 and 90 patients with late-onset Alzheimer's over the age of 65 from 1997 to 2007 for memory symptoms and clinical characteristics, Koedam et al. (2009) claimed that the mean age of the early-onset group was 56 years old, and the late-onset group was 74 years old (p. 1). Koedam et al. (2009) also stated that the early-onset group often presented with a non-memory phenotype but had apraxia or impaired motor skills as the most presenting symptom (p. 1). Koedam et al. (2009) reported that one-third of the early-onset patients presented with non-memory impairment compared to the 6% of late-onset patients with a p-value less than 0.001 (p. 3). In addition, Koedam et al. (2009) stated that apraxia was the most frequent symptom with 12%, then language impairment with 9%, and then aphasic-apraxia agnosia syndrome with 8% while these symptoms occurred in the late-onset patients with less than 2% (p. 3).

Alzheimer's may occur in individuals as early onset and may not have evident biomarkers for cognitive decline. However, Koedam et al. (2009) reported that the mean early onset age was fifty-six years old. Rodrigue et al. (2021) reported that the concentration of Aβ rapidly increased after the age of sixty. Both target age groups are in the range of a senior citizen, which may be considered elderly, if not reaching elderly. Therefore, the green tea mouthwash may be implemented into the routine of young adults aged 20 to 30 as the mouthwash may be most effective at that age since the risk of developing severe periodontitis, plaque, and Aβ concentration is not as increased at that age group. Young adults may not be at elevated risk for the development of the key components that lead to Alzheimer's and therefore, they may be able to decrease the risk of developing the disease before they reach an age where treatment may not be as effective.

Conclusion

The properties and mechanism of the catechins of green tea mouthwash suggest that implementing green tea mouthwash into the dental care of young adults may be an effective method to reduce the risk of developing Alzheimer's disease. The studies of green tea mouthwash reducing oral bacteria, proinflammatory cytokines, cognitive deficits, and plaque could suggest that the mouthwash may be effective and beneficial towards reducing the mechanisms of *P. gingivalis.* However, green tea mouthwash may need to be utilized daily to be effective where individuals rinse with the mouthwash once or twice a day in addition to their daily oral hygiene routine. Alternatively, green tea may also be consumed orally as a drink multiple times a day to produce the same benefits as green tea mouthwash. Other teas such as red and black tea that may produce similar cognitive benefits to green tea should also be researched further to determine if different teas can also benefit the oral cavity and therefore, prevent the risk of Alzheimer's.

However, an experiment analyzing the efficiency of green tea mouthwash reducing the risk of Alzheimer's due to its catechins may confirm green tea's benefits. This experiment may be beneficial to Alzheimer's disease and dental community given that Alzheimer's has no current cure. Reducing the risk of

Alzheimer's may lower the direct and indirect costs of disease and overall reduce the rate of older adults in the United States that develop and die due to this neurodegenerative disease. By proposing a proactive measure to prevent Alzheimer's, the development of herbal mouthwash may be promoted by dentists for their patients. Green tea mouthwash may ultimately build a relationship between the dental and Alzheimer's community, promoting the benefits of oral hygiene for both the oral cavity and the brain.

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