Zymenta and Cerelist: A novel approach to nutritional management of cholinergic deficiency

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ABSTRACT

Age-related cognitive decline adversely affects a significant portion of the population. Studies have suggested that cognition may be maintained by supporting cholinergic function and overall brain health. Zymenta and Cerelist are nutritional supplements that address nutritional deficiencies that may be related to mild cognitive decline by providing complementary ingredients to 1) support acetylcholine (Ach) synthesis; 2) reduce ACh breakdown; and 3) protect neuronal cell structure and function. This article reviews the health implications of a cholinergic deficit in patients with cognitive complaints and describes how the ingredients in Zymenta and Cerelist provide a unique, integrative approach to support of healthy cognitive function.

INTRODUCTION

Mild cognitive decline can be a normal part of the aging process. These cognitive challenges may be improved by supporting cholinergic function and overall brain health. Damage to cholinergic neurons is a prominent cause of memory loss. Damage to brain cells appears to disproportionately target cholinergic neurons (Pinto et al., 2011), which innervate all areas of the brain. Injury to these cells, and consequent reduction in acetylcholine (ACh) levels, contribute to a diversity of symptoms, including cognitive and functional decline. Thus, interventions that support cholinergic activity of the brain may help manage symptoms of memory loss associated with aging.

Zymenta and Cerelist are nutritional supplements designed to offer nutritional support to maintain proper function of the cholinergic nervous system. These products provide nutrients that are essential for cholinergic activity and brain health, which are found to be lacking in the diets of up to 90% of American adults (Werder 159-95; Zeisel and da Costa 615-23). These nutritional deficiencies can exacerbate neurological impairments and minimize the efficacy of interventions targeting cholinergic activity (Werder 159-95; Zeisel and da Costa 615-23; Zeisel). By providing these nutrients in combination with other cholinergic-supporting ingredients, these products offer a multidimensional approach to managing cognitive changes that occur as a part of aging. This article explains the rationale behind Cerelist and Zymenta and summarizes how these products’ ingredients offer cholinergic support for patients with mild memory loss.

ZYMENTA and CERELIST – Multiple approaches to cholinergic support

Supporting cholinergic health is important in patients with cognitive complaints. Primary contributors to cholinergic dysfunction are reduced synthesis, increased degradation, and impaired signaling of ACh, a critical neurotransmitter in the brain that facilitates cognitive and functional activities. A common approach to medically managing cholinergic function involves inhibiting the enzymatic breakdown of ACh, thereby prolonging its half-life. However, the cholinergic benefits of blocking ACh breakdown may be reduced or negated if ACh synthesis is low or receptor activity is impaired. In addition to reducing the degradation of ACh, mechanisms of action that support its synthesis or increase receptor activity will help further support cholinergic function.

Extending the half-life of ACh, naturally

Plant-derived methods for reducing the breakdown of ACh, have been in use for centuries. Zymenta provides a standardized amount of Huperzine A (HupA) a potent and reversible way to block ACh breakdown, derived from the Chinese club moss Huperzia serrata. HupA has high bioavailability and easily crosses the blood-brain barrier (Wang et al. 457-65; Fu and Li). It is also highly specific for the predominant acetylcholinesterase isomorph in the human brain (Wollen 223-44) and has been shown in several clinical trials to improve cognitive function (Wang et al. 457-65; Fu and Li). In addition, HupA, presumably through its ACh-supporting effects, has been shown to protect against the formation of β-amyloid plaques (Zhang, Yan, and Tang 173-83; Wang, Yan, and Tang 1-26; Fu and Li), prevent glutamate excitotoxicity (Wang, Yan, and Tang 1-26), and reduce...
cytokine production (Swardfager et al.). Thus, HupA provides multidimensional benefits for nutritional management of mild cognitive decline. HupA has minimal peripheral effects, and evidence suggests that it is both effective and well tolerated (Wang et al. 649-64).

Due to the HupA content, Zymenta is not recommended for people using interventions that block ACh activity. Cereplast does not contain Hup A and is a great alternative to Zymenta in order to provide the needed nutritional support for patients with cognitive decline.

Choline – an ACh precursor in limited supply

If systemic choline is low, the body may meet certain metabolic demands by removing choline from neuronal cell membranes (Ulus et al. 217-27), upregulating acetylcholinesterase activity, or reducing activity of choline acetyltransferase, the enzyme that joins choline and acetyl-CoA to form ACh (Liapi et al. 269-76). All of these actions may result in reduced availability of choline for ACh synthesis, thereby counteracting the potential benefits of interventions that reduce the breakdown of ACh. Therefore, choline supplementation should be considered to ensure adequate choline availability for ACh synthesis.

Choline is an essential nutrient necessary for lipoprotein transport throughout the body, methylation reactions, maintenance of cellular membrane integrity, and normal liver and muscle function (Zeisel and da Costa 615-23). In the brain, choline is a component of phospholipids that are necessary for structure and function of healthy brain cells. Choline is also an essential precursor for the synthesis of ACh, the central cholinergic neurotransmitter necessary for various dimensions of cognitive function, including learning, recalling, computing, and performing routine activities.

Adequate dietary choline intake is essential for health as low choline availability has been shown to lead to liver, heart, immune and muscle dysfunction (Zeisel). Low choline is also associated with neurological impairments, including impaired cognitive performance (Kochunov et al. 1190-99). Non-modifiable factors including age, gender, and genetics influence the risk for developing choline deficiency symptoms. Premenopausal women tend to be at lower risk for choline deficiency compared to men and post-menopausal women due to a protective effect of estrogen on choline status (Resseguie et al. 2622-32). However, as much as 50% of the population carries single nucleotide polymorphisms that markedly increase the risk of choline deficiency, regardless of estrogen status (Kohlmeier et al. 16025-30; da Costa et al. 1336-44; Ivanov et al. 313-18; Niculescu and Zeisel 2333S-5S; Zeisel). Choline requirements and risk of deficiency can also increase when intake or absorption of certain B-vitamins, such as folate or vitamin B12, is low (Jacob et al. 712-17; Niculescu and Zeisel 2333S-5S; Ivanov et al. 313-18; Kohlmeier et al. 16025-30), which is not uncommon among aging populations (Werder 159-95). Moreover, choline deficiency symptoms may be precipitated when illness or hospitalization results in limited food intake. Despite these findings, little attention has been given to the importance of achieving adequate choline intake for maintaining neurological and overall health (Zeisel and da Costa 615-23).

Human endogenous production of choline is insufficient to meet metabolic demands, and therefore we rely chiefly on dietary intake for the majority of our choline. However, most American diets contain few concentrated food sources of choline, with the exception of eggs. In addition, choline is not commonly used in food fortification or in multivitamin preparations typically intended to bridge nutrient gaps. Thus, achieving sufficient choline intake through food consumption can be challenging for individuals, particularly those following diets that limit calories, fat, cholesterol, or animal products, or for those avoiding certain foods.

Studies have shown that many individuals require choline intake at amounts well above current recommendations in order to reverse deficiency symptoms (Sha et al. 2962-75; Fischer et al. 1275-85). This has led to a recent proposal that the recommended Adequate Intake for choline be increased (Zeisel and da Costa 615-23). Yet, with approximately 90% of American adults already failing to meet the Adequate Intake (Zeisel and da Costa 615-23; Bidulescu et al. 14; Sha et al. 2962-75; Fischer et al. 1275-85), recommendations to increase choline intake will have little effect unless awareness and dietary distribution improve.

Choline intake in adults is inversely related to age, with individuals over age 70 averaging less than half of the recommended Adequate Intake per day (Zeisel and da Costa 615-23). Given the risk factors for choline deficiency and the challenges to meet demands from dietary sources, choline supplementation to support ACh synthesis is indicated for patients with cholinergic impairments. While not all studies support the benefits of choline supplementation for cognitive performance (Kidd 85-115), studies showing increased brain choline concentration (Babb et al. 248-54; Babb et al. 1-9), preservation of cell membrane structure (Zhao, Frohman, and Bluszczajn 16), and stimulation of ACh production (Ulus et al. 217-27) in response to

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exogenous choline support the contention that choline is essential for healthy neurological function (Parnetti et al. 159-64).

Zymenta and Cerelist each include two forms of choline to support the body’s choline needs. Choline bitartrate helps ensure overall adequate choline supply, so total body demands can be met without drawing from the central nervous system supply. Alpha-glycerylphosphorylcholine (α-GPC) provides choline in a form that readily crosses the blood-brain barrier to meet central cholinergic demands. In addition, Zymenta and Cerelist contain acetyl-L-carnitine, which provides an acetyl group for the formation of ACh in the brain. In the central nervous system, the enzyme choline acetyltransferase facilitates the synthesis of ACh from acetyl-L-carnitine and α-GPC (Nalecz and Nalecz 597-609). These products also contain folate, vitamin B12, and vitamin B6, which have all been found to modulate choline metabolism.

**Nutrients to protect brain cell structure and function**

The brain is a region of high metabolic activity that yields free radicals which, with advanced age, exceed the brain’s antioxidant capacity. The resultant oxidative damage, in combination with sustained presence of immune system activity, promotes the continuation of cellular damage. Therefore, an additional means by which Zymenta and Cerelist support cholinergic activity and overall brain health is by providing ingredients that help conserve the structural integrity and promote healthy metabolic functions of brain cells.

For example, HupA, found in Zymenta, has been shown to increase neuronal growth factor which stimulates generation of new neurons (Zhang, Yan, and Tang 173-83; Wang, Yan, and Tang 1-26). Choline is not only a precursor for ACh, but also a structural and functional component of cellular membranes, helping to maintain integrity of brain cells. In addition, choline and the B vitamins are involved in DNA methylation pathways and, as such, support cellular function and replication (Coppede 246-60; Mason 941S-75). Choline and B vitamins can also lower elevated homocysteine. (Werder 159-95). In addition to its role as an acetyl donor for ACh synthesis, acetyl-L-carnitine is an intermediate necessary for cellular energy metabolism.

Zymenta and Cerelist also contain α-lipoic acid which, like α-GPC and acetyl-L-carnitine, readily crosses the blood-brain barrier. Once in the brain, it supports brain cell metabolism by enhancing insulin sensitivity and promoting brain glucose uptake. (Maczurek et al. 1463-70). Lipoic acid has also been shown to activate choline acetyltransferase activity to promote ACh synthesis (Maczurek et al. 1463-70). In addition, α-lipoic acid provides neuroprotective effects (Goraca and slanowicz-Antkowski 141-46; Saed et al. e2459), prevents deleterious age-associated changes in brain cell gene expression (Park et al. 484-95). α-Lipoic acid also acts synergistically with acetyl-L-carnitine to scavenge free radicals for neuronal protection (Aliev et al. 320-33; Hagen et al. 1870-75; Liu et al. 2356-61; Long et al. 755-63; Shenk et al. 199-206; Abdul and Butterfield 371-84) and the enhancement of cognitive performance (Milgram et al. 3756-62; Liu et al. 2356-61; Shenk et al. 199-206).

**SUMMARY**

Age-related cognitive decline adversely affects a significant portion of the population. Studies have demonstrated that cognition and overall brain health may be improved by supporting cholinergic function. However, widespread nutritional deficits may hinder the therapeutic potential of existing pharmaceutical compounds. To address this need, Zymenta and Cerelist have been formulated to nutritionally manage cholinergic activity through a unique and complementary three-pronged approach that provides: 1) ACh precursors to support its synthesis; 2) protective nutrients to support brain cell integrity and function; and 3), a natural potent plant extract to prolong ACh half-life (not found in Cerelist). By addressing under-recognized, highly prevalent nutritional deficits, Zymenta and Cerelist may offer a beneficial therapeutic edge to patients with mild cognitive decline associated with aging, or those who wish to support healthy overall brain function.

**References**


