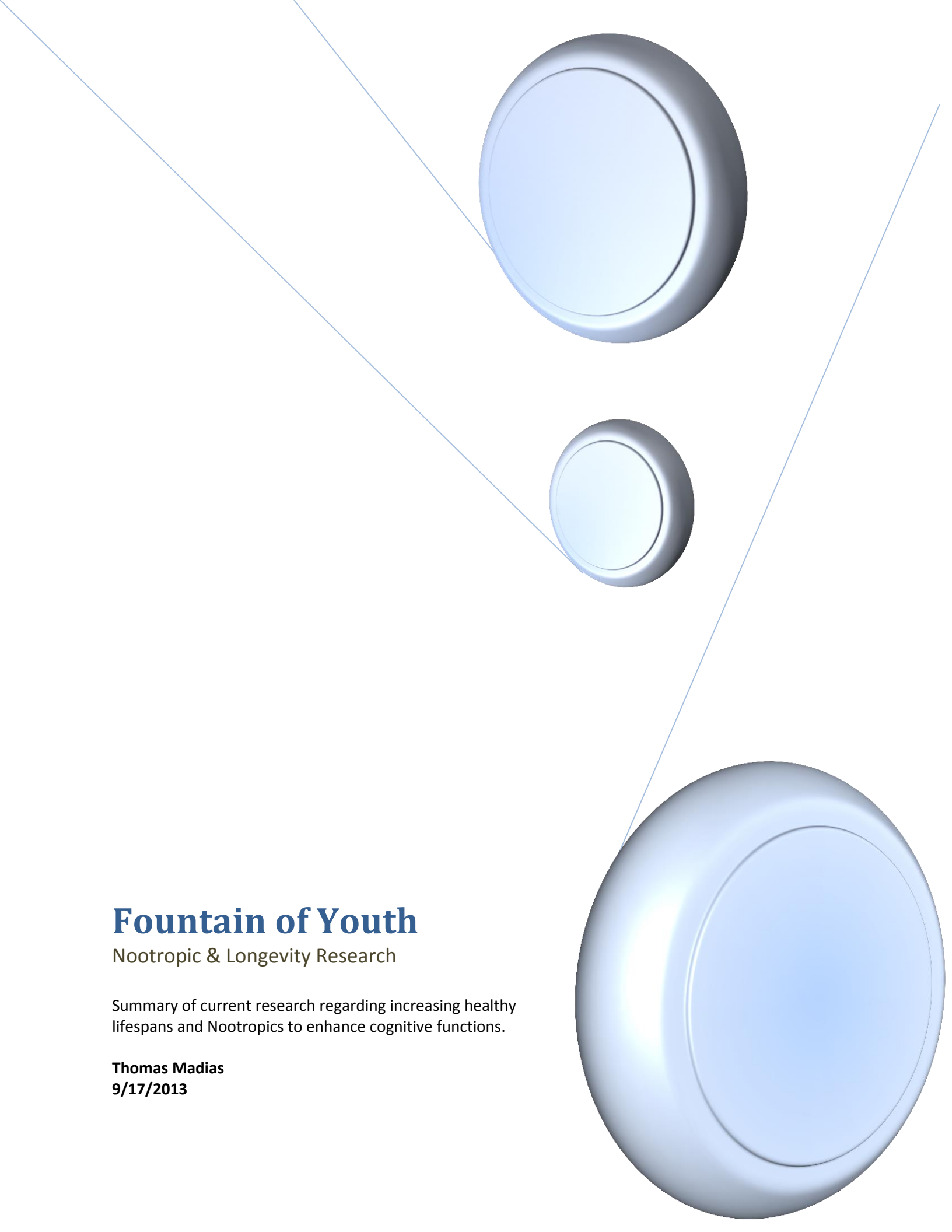

Fountain of Youth

Nootropic & Longevity Research

Summary of current research regarding increasing healthy lifespans and Nootropics to enhance cognitive functions.

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9/17/2013

Fountain of Youth

Dating back centuries Kings and Sages have pondered the question of eternal youth and how to attain it. Combining the scientific technology of today with the knowledge passed on by those searching, people are now able to find more ways to extend their youthful lifespan than ever before. Which the ideal place to focus on, as not many would want to live longer if it meant extending the time you are unable to enjoy your life due to you losing the ability due to deteriorating health.

POWERFUL ANTIOXIDANT RESVERATROL

Resveratrol has been shown to extend the maximum and healthy lifespan of several animals in studies, as well as have great health benefits through restricting bad calories. In rodents, caloric restriction slows aging and extends lifespan. At least 4 studies have shown that caloric restriction reduces 8-OHdG damages in various organs of rodents. One of these studies (Hamilton et al., 2001) showed that caloric restriction reduced accumulation of 8-OHdG with age in rat brain, heart and skeletal muscle, and in mouse brain, heart, kidney and liver. More recently, Wolf et al. (2005) showed that dietary restriction reduced accumulation of 8-OHdG with age in rat brain, heart, skeletal muscle, and liver. Thus reduction of oxidative DNA damage is associated with a slower rate of aging and increased lifespan. Since resveratrol restricts calories without requiring people to eat less, this is one way resveratrol likely extends life span.

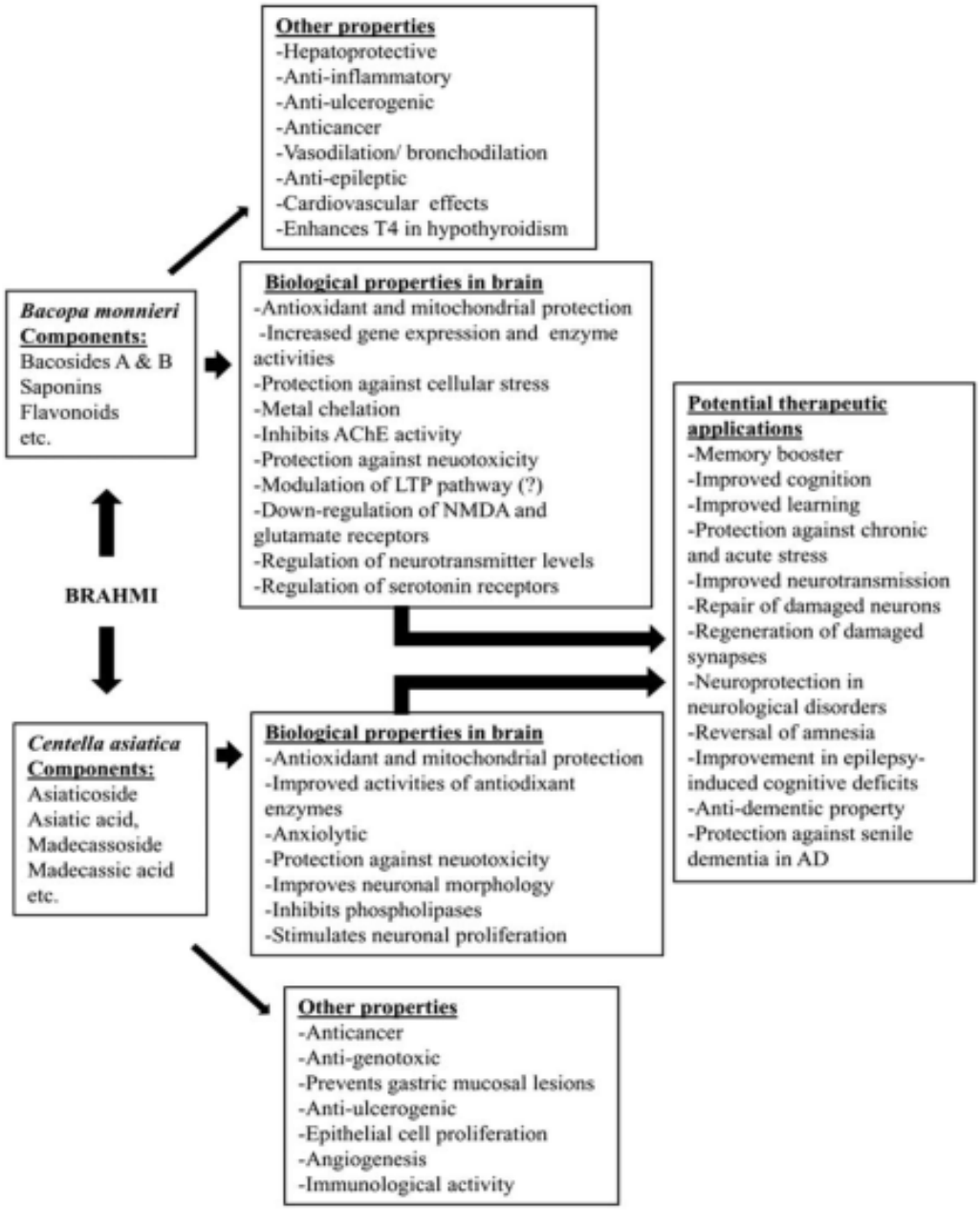
Aurvedic Medicine

While some where attempting Alchemy in their attempts to attain internal youth, Indian Medicinal Sages have passed down their research into plants to extend their healthy lifespan through herbal preparations of Ayurvedic. The drugs promoting medha (intellect) are termed as medhya drugs. Ayurvedic System of Medicine has mentioned several naturally occurring medicinal plants under the category 'Medhya' .

Ayurveda is the traditional healing modality of the Vedic culture from India. It is said to be 2000 to 5000 years old, meaning it has stood the test of time. Ayurveda is a Sanskrit word that literally translates as “the wisdom of life” or “the knowledge of longevity”. In accordance with this definition, Ayurvedic medicine views health as much more than the absence of disease. The wise seers and sages of the time, intuitively understanding the physiology and workings of the mind-body-spirit long before the advents of modern medicine, explained the basic principles of Ayurveda.

By virtue of inducing mental upliftment as major influence several medicinal plants mentioned as 'Rasayan Drugs' in Ayurveda are primarily claimed as 'medhya' . Further there is a special class of some Rasayan drugs called 'Medhya Rasayan' which is supposed to be having specific influence on higher brain functions.

'Brahmi'(Bacopa monniera) and 'Vacha' (Acorus calamus) are the important plants in the group 'Medhya Rasayana'.



They are widely claimed as restorative, nerving and mental tonics. They have got prominent action on Central Nervous System where they improve grasping power, memory, intellect and speech, and correct aberrations of emotions, mood and personality of an individual.

The benefits of Ayurvedic medicine have been proven over centuries of use, and through modern science the benefits of many Ayurvedic medicines have been confirmed

Changes the brain incurs with age

In addition to the structural changes that the brain incurs with age, the aging process also entails a broad range of biochemical changes. More specifically, neurons communicate with each other via specialized chemical messengers called neurotransmitters. Several studies have identified a number of these neurotransmitters, as well as their receptors, that exhibit a marked alteration in different regions of the brain as part of the normal aging process.

Dopamine

An overwhelming number of studies have reported age-related changes in dopamine synthesis, binding sites, and number of receptors. Studies using positron emission tomography (PET) in living human subjects have shown a significant age-related decline in dopamine synthesis,[21] notably in the striatum and extrastriatal regions (excluding the midbrain).[22] Significant age-related decreases in dopamine receptors D1, D2, and D3 have also been highly reported.[23][24][25][26][27] A general decrease in D1 and D2 receptors has been shown,[25] and more specifically a decrease of D1 and D2 receptor binding in the caudate nucleus and putamen.[24][27] A general decrease in D1 receptor density has also been shown to occur with age. Significant age-related declines in dopamine receptors, D2 and D3 were detected in the anterior cingulate cortex, frontal cortex, lateral temporal cortex, hippocampus, medial temporal cortex, amygdala, medial thalamus, and lateral thalamus[23] One study also indicated a significant inverse correlation between dopamine binding in the occipital cortex and age.[24] Postmortem studies also show that the number of D1 and D2 receptors decline with age in both the caudate nucleus and the putamen, although the ratio of these receptors did not show age-related changes.[26] The loss of dopamine with age is thought to be responsible for many neurological symptoms that increase in frequency with age, such as decreased arm swing and increased rigidity.[28] Changes in dopamine levels may also cause age-related changes in cognitive flexibility.[28]

Serotonin

Decreasing levels of different serotonin receptors and the serotonin transporter, 5-HTT, have also been shown to occur with age. Studies conducted using PET methods on humans, in vivo, show that levels of the S2 receptor in the caudate nucleus, putamen, and frontal cerebral cortex, decline with age.[27] A decreased binding capacity of the 5-HT2 receptor in the frontal cortex was also found,[25] as well as a decreased binding capacity of the serotonin transporter, 5-HHT, in the thalamus and the midbrain.[29] Postmortem studies on humans have indicated decreased binding capacities of serotonin and a decrease in the number of S1 receptors in the frontal cortex and hippocampus as well as a decrease in affinity in the putamen.[30]

Glutamate

Glutamate is another neurotransmitter that tends to decrease with age.[31][32][33] Studies have shown older subjects to have lower glutamate concentration in the motor cortex compared to younger subjects[33] A significant age-related decline especially in the parietal gray matter, basal ganglia, and to a lesser degree, the frontal white matter, has also been noted.[31][32] Although these levels were studied in the normal human brain, the parietal and basal ganglia regions are often affected in degenerative brain diseases associated with aging and it has therefore been suggested that brain glutamate may be useful as a marker of brain diseases that are affected by aging.[31]

Pathological effects of poor DNA repair

Experimental animals with genetic deficiencies in DNA repair often show decreased life span and increased cancer incidence.[15] For example, mice deficient in the dominant NHEJ pathway and in telomere maintenance mechanisms get lymphoma and infections more often, and, as a consequence, have shorter lifespans than wild-type mice.[41] In similar manner, mice deficient in a key repair and transcription protein that unwinds DNA helices have premature onset of aging-related diseases and consequent shortening of lifespan.[42] However, not every DNA repair deficiency creates exactly the predicted effects; mice deficient in the NER pathway exhibited shortened life span without correspondingly higher rates of mutation.[43]

If the rate of DNA damage exceeds the capacity of the cell to repair it, the accumulation of errors can overwhelm the cell and result in early senescence, apoptosis, or cancer. Inherited diseases associated with faulty DNA repair functioning result in premature aging,[15] increased sensitivity to carcinogens, and correspondingly increased cancer risk (see below). On the other hand, organisms with enhanced DNA repair systems, such as Deinococcus radiodurans, the most radiation-resistant known organism, exhibit remarkable resistance to the double-strand break-inducing effects of radioactivity, likely due to enhanced efficiency of DNA repair and especially NHEJ.[44]

Longevity and caloric restriction

Most life span influencing genes affect the rate of DNA damage

A number of individual genes have been identified as influencing variations in life span within a population of organisms. The effects of these genes are strongly dependent on the environment, in particular, on the organism's diet. Caloric restriction reproducibly results in extended lifespan in a variety of organisms, likely via nutrient sensing pathways and decreased metabolic rate. The molecular mechanisms by which such restriction results in lengthened lifespan are as yet unclear (see[45] for some discussion); however, the behavior of many genes known to be involved in DNA repair is altered under conditions of caloric restriction.

For example, increasing the gene dosage of the gene SIR-2, which regulates DNA packaging in the nematode worm Caenorhabditis elegans, can significantly extend lifespan.[46] The mammalian homolog of SIR-2 is known to induce downstream DNA repair factors involved in NHEJ, an activity that is especially promoted under conditions of caloric restriction.[47] Caloric restriction has been closely

linked to the rate of base excision repair in the nuclear DNA of rodents,[48] although similar effects have not been observed in mitochondrial DNA.[49]

It is interesting to note that the C. elegans gene AGE-1, an upstream effector of DNA repair pathways, confers dramatically extended life span under free-feeding conditions but leads to a decrease in reproductive fitness under conditions of caloric restriction.[50] This observation supports the pleiotropy theory of the biological origins of aging, which suggests that genes conferring a large survival advantage early in life will be selected for even if they carry a corresponding disadvantage late in life.

Advanced glycation end-product

An advanced glycation end-product (AGE) is the end result of a chain of chemical reactions involving an initial glycation reaction. AGES are well-known for their formation in Diabetes, but also occur in other disease processes.

An AGE is the result of a chain of chemical reactions after an initial glycation reaction, which refers to the addition of a carbohydrate without the involvement of an enzyme. Intermediate products in the formation of an AGE are known as Amadori, Schiff base, and Maillard products, named after the researchers who first described them.

Outside of the body (exogenously), AGEs may be formed by heating (e.g., cooking);.[2][3] Inside the body (endogenously) AGEs may be formed as a result of normal metabolism and aging.

Under certain pathologic conditions, such as oxidative stress due to hyperglycemia in patients with diabetes,[4] and hyperlipidemia[citation needed], AGE formation can be increased beyond normal levels. AGEs are now known to play a role as proinflammatory mediators in gestational diabetes as well.[5]

Formation in Diabetes

In diabetes, in cells unable to reduce glucose intake (e.g., endothelial cells), hyperglycemia results in higher intracellular glucose levels.[4] [6][7] Higher intracellular glucose levels result in increased levels of NADH and FADH, increasing the proton gradient beyond a particular threshold at which the complex III prevents further increase by stopping the electron transport chain.[8] This results in mitochondrial production of reactive oxygen species, activating PARP1 by damaging DNA. PARP1, in turn, induces ADP-ribosylation of GAPDH, a protein involved in glucose metabolism, leading to its inactivation and an accumulation of metabolites earlier in the metabolism pathway. These metabolites activate multiple pathogenic mechanisms,[which?] one of which includes increased production of AGEs.

Examples of AGE-modified sites are carboxymethyllysine (CML), carboxyethyllysine (CEL), and Argpyrimidine, which is the most common.

Formation in other diseases

The formation and accumulation of advanced glycation endproducts (AGEs) has been implicated in the progression of age-related diseases.[9] AGEs have been implicated in Alzheimer's Disease,[10] cardiovascular disease,[11] and stroke.[12] The mechanism by which AGEs induce damage is through a process called cross-linking that causes intracellular damage and apoptosis.[13] They form photosensitizers in the crystalline lens,[14] which has implications for cataract development.[15] Reduced muscle function is also associated with AGEs.[16]

Potential therapeutic interventions for AGE formation

AGEs are the subject of ongoing research. There are three therapeutic approaches: preventing the formation of AGEs, breaking AGE crosslinks after they are formed, and preventing negative effects of AGEs.

Compounds that are thought to inhibit AGE formation, at least in vitro, include Vitamin C,[29] benfotiamine, pyridoxamine, alpha-lipoic acid,[30] taurine,[31] pimagedine,[32] aspirin,[33][34] carnosine,[35] metformin,[36] pioglitazone,[36] and pentoxifylline.[36]

Compounds that may prevent negative effects of AGEs, at least in vitro, include resveratrol.[37]

Compounds that are thought to break some existing AGE crosslinks include Alagebrium (and related compounds ALT-462; ALT-486; ALT-946)[38] and N-phenacyl thiazolium bromide.[39]

However, there is no agent known that can break down the most common AGE, glucosepane, which appears 10 to 1000 times more commonly in human tissue than any other cross-linking AGE.[40][41]