The Blueberry Effect

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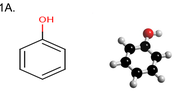
Abstract:

Blueberries (BB) contain high levels of antioxidants called anthocyanins. This class of compounds helps prevent increasing cell death and disease that otherwise are likely to be caused by free radicals generated with age. Peer reviewed scientific studies were reviewed to determine the effect of blueberry supplementation on human and animal cognitive and motor functions. My hypothesis was that I could use the conclusions of these studies to determine an ideal daily dosage of BB that one should consume to maximize one's health and longevity. One study found that supplementing the diet of rats with 2% (approximately 1/2 a cup daily for humans) BB decreased cognitive and motor decline by altering cell signaling and protecting from free radicals. Another study found that these effects were strengthened by increasing the flavonoid juice concentration to between 10 and 50%. In human studies, similar results were found, with the maximum cognitive improvements at 37 mg flavonoids/day in one study. While not enough human studies have been done to allow an accurate determination of an ideal daily dosage of blueberries, these studies indicate that up to ½ cup BB/day, or up to 37 mg flavonoids/day (including 50% juice drinks) is both safe and beneficial.

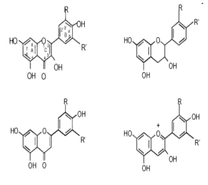
Introduction:

Blueberries (BB) contain high levels of antioxidants, which help prevent against cell death by free radicals (5). Free radicals are unpaired electrons in the outer shell of atoms, formed as a result of oxidation reactions that occur during cellular respiration. As electrons pass through carriers in the electron transport chain, they lose energy, but many free radicals fly out of the chain. These unpaired electrons are unstable and volatile, thus they start chain reactions damaging other molecules like DNA. For instance, the telomeres on chromosomes shorten and stop protecting cell DNA, damaging and eventually causing cell death or cancer. The body has natural antioxidants to protect from free radicals. These include enzymes, such as peroxidases, superoxide dismutase, and catalase. Antioxidants get rid of free radical intermediates so that the destructive chain reactions are broken, and they prevent more oxidation reactions by becoming oxidized. They play the role of the reducing agent in the oxidation reaction, meaning they give an electron to another atom to complete its outer shell. As time goes on, however, more oxidation reactions have occurred, meaning there are more free radicals generated. External sources like the sun also create free radicals over time. The body's natural antioxidants become overwhelmed by the number of free radicals very early in life, a state known as Oxidative stress. With increasing cell damage the body becomes chronically inflamed in its attempt to heal the injured cells. Though the free radicals are attacked, this constant state of warfare also wears on the body, eventually causing the cells more damage than benefit (1). It is therefore necessary to supplement one's natural antioxidants with nutrient antioxidants, gained through consuming food such as whole grains, fruits and vegetables. (9)The antioxidants BB contain are called anthocyanins (1). Anthocyanins are pigments found in plants that belong to the molecular class flavonoids (2), which are polyphenolic compounds. Polyphenols contain many units of the phenol unit building blocks, also called carbolic acid (4). With the formula, C_6H_5OH , phenol units are made up of a hydroxyl group bonded to a phenyl ring. This is called an aromatic compound (3). Anthocyanins are very strong antioxidants because they contain multiple aromatic rings in which to catch free radicals (1). The darker a food is, the more polyphenols it contains that can trap free radicals, which is why BB, with their dark blue color, are so beneficial. This poster presents the results of selected studies about BB and other flavonoid supplementation in both humans and animals. My hypothesis is that I can use these studies to determine an ideal daily dosage of BB that one should consume to maximize one's health and longevity.

1A.



1B.



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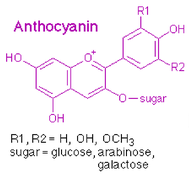

Figure1:
Structures related to anthocyanins
1A. Phenol
1B. Flavonoids
1C. Anthocyanin

Figure 2: Telomeres

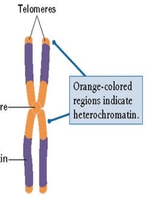

Figure 3:

Foods containing high levels of anthocyanins : This chart shows that blueberries have a very high concentration of anthocyanins. Although other sources do have higher concentrations, this poster does not intend to compare the varying benefits of different sources, but rather to focus only on the effects of blueberries (1)

Food Source	Anthocyanin Content in mg per 100 g
Acai	320
blackcurrant	190-270
chokeberry	1,480
eggplant	750
orange	200
Marion blackberry	317
black raspberry	589
raspberry	365
wild BB	558
Cherry	340-400
redcurrant	80-420
red grape	888
red wine	24-35
purple corn	1,642

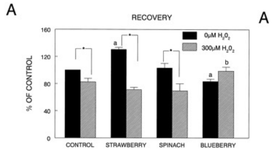

Figure4: Calcium recovery

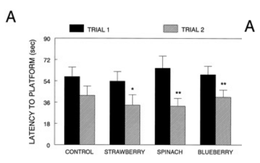

Figure5: Morris Water Maze Performance

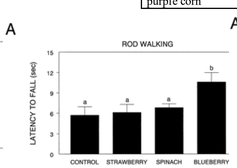

Figure6: Rod walking/Rotary Performance (motor skills)

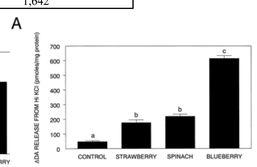

Figure7: carbachol-stimulated GTPase activitiy, oxotremorine-enhanced K+ -ERDA

Method:

I looked at scientific peer reviewed literature to obtain data, and non-commercial websites to obtain general background information. Three studies by James A. Joseph et al. (5-7) were used. However, as the data from these studies were primarily from rats, a study on humans was also used (8).

Results:

Many studies have tested the effects of BB (and other flavonoid) supplementation on the cognitive and motor abilities of animals (primarily rats), to see if age-related decline in these abilities can be slowed or reversed. In each study, BB supplementation was 2% of the rats' diet, for 8-12 weeks (5-7). Some of the tests were conducted on older rats, about 19 months old (6), while others used rats ranging from 6 to 15 months. Young rats were used for a radiation test (5), while young transgenic mice were used to test for Alzheimer's (6). The radiation test consisted of exposing the rats to Fe irradiation (1.5 Gy at 1 GeV) after they were given a flavonoid supplement, with the knowledge that radiation causes cognitive decline resulting from programmed stem cell death (5). The tests used to access the rats' cognitive and motor abilities were the Morris Water Maze or radial foot-shocking arm maze, which tested the rats' spatial awareness and object recognition skills, the rod walking or accelerating rotarod test, which tested balance and coordination, and an inhibitory avoidance task, which tested object recognition and memory (7). All maze tests accessed the learning/acquisition, short term (working) and long term (reference) memory of the rats. Reference memory deals with the constants in the mazes' rules, whereas working memory requires the rats to remember specific details that may change between tasks (6).

Though they varied slightly in design (some studies compared blueberries to other flavonoids), the three studies I selected all concluded that BB supplementation of aged rats reverses cognitive decline, aids motor skills, and alters cell signaling (6). [See Figs. 4-7 of (10)]. The authors of these studies concluded that the changes in signaling were the key to the resulting cognitive and motor benefits. They found that the polyphenolic properties of BB increased rats' neuronal signaling by augmenting the sensitivity of their muscarinic receptors, consequently shown in a reversal of cognitive damages. [Fig.5 of (10)] This included improvements in object recognition (11). The polyphenols were also found to decrease dysfunctional signaling such as stress signals, through improving calcium regulation, which typically decreases with age [Fig.4:)]. In addition, BB supplementation was found to increase rats' striatal and hippocampal protein kinases, which are important in making short term memories into long term memories (7) [Fig.7 of (10)]. The activation of these signals affects signaling pathways during transcription, thus allowing new protein, especially mitogen-activated protein kinase, to be synthesized, so that new memories can be formed (5). The signaling also helped to regulate an insulin-like growth factor that improved rat's spatial learning in these studies (7).

In one study(5), the rats were exposed to radiation that was known to cause spatial working memory deficits. However, it was found that BB supplementation provided a buffer against these harmful effects, allowing improved striatal functioning and hippocampus plasticity. This protection was concluded to result from BB scavenging of free radicals generated by the radiation. Such free radical generation also occurs simply through normal aging.

In humans, similar results have been obtained, though there have been fewer studies. Of the two studies found, Krikorian et al. (12) found that humans experienced cognitive improvement with 12 weeks of BB supplementation, specifically in intrusion errors, paired association learning, and list recall. The amount of BB supplementation was not given, although this study was meant to be comparable to a similar study done with grape juice, in which 10-50% grape juice was supplemented (5). In the second study, Letenneur *et al* (10) found that when participants' flavonoid intake (including BB and other polyphenols) increased, their cognitive function also increased. Participants were followed up over 5-10 yrs. The average flavonoid intake was 14.33 mg/day, and factors such as age, sex, and education were adjusted for. The MMSE cognitive test was used to assess participants, and a mean score of 27.1 was obtained. The highest flavonoid intake by participants was 26.94 mg/day, and they had the highest score on the MMSE (Fig. 4). Higher flavonoid intake was also found to reduce participants' risk of many age-related diseases such as cancer, Alzheimer's, and cardiovascular disease (8). Another study noted that while not all flavonoids have been shown to be correlated to equal improvements in human motor abilities, BB are among those that have been. Detailed analysis of human motor abilities after supplementation was not given, however (7).

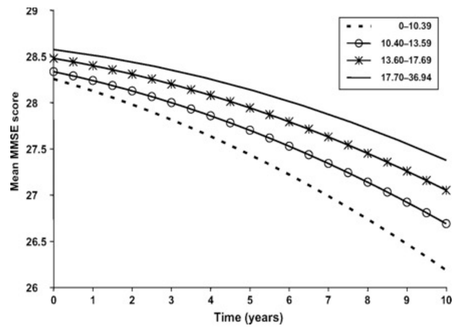

Figure 4: Graph of Evolution of the mean MMSE score for participants with varying flavonoid consumption levels. The mini-mental state examination (MMSE) is a brief 30-point questionnaire that is used to screen for cognitive function. (Key represents participants' flavonoid consumption levels in mg) This graph shows that while all participants' cognitive scores declined with age, those who consumed the most flavonoids (the solid line) always had the highest scores. (8)

Discussion:

Figure 4 reviews results that show while all participants' cognitive scores declined with age, those who consumed the most flavonoids (the solid line) always had the highest scores (8).

Multiple animal studies have shown the positive effect that BB supplementation has on reducing age-related cognitive and motor decline. The human studies that have been done agree with this conclusion, although it is important to note that fewer intervention studies have been done with humans, and observational studies can sometimes result in unreliable data (7). Also, the human studies from which data were obtained did not provide a clear suggestion for the optimal level of BB supplementation in humans. They did not report any harmful consequences for even the highest tested level of flavonoid consumption at 37 mg (8). Since grape juice and BB supplementation had comparably positive effects in the two human studies, it can hypothesized that the recommended value of flavonoid consumption would be equal to that for BB consumption. These studies have shown that 2% BB in animals' diets is beneficial, as is at least 50% flavonoid-containing juice. Therefore, it can be hypothesized that including 2% (1/2 cup) BB or comparable flavonoids in the diet (such as through consuming drinks that are at least 50% juice) could be a desirable minimum daily recommendation for humans (5). In addition, up to 37 mg of flavonoids could be beneficial. Although the study on flavonoid intake indicates that higher supplementation is not likely to be harmful (10), caution is recommended due to the lack of data on flavonoid intake higher than 37 mg, and the fact that this data is not specific to BB. (The flavonoid content of BB varies greatly, ranging from 2.5-388mg/100 g fresh weight (13). The advantages of following a minimum daily recommendation should not be minimized, however, until more human studies on BB are done. It is recommended that people also use other strategies to slow their aging process, such as following other good diet practices, exercising both physically and cognitively, and taking care of their mental health.

Conclusion:

Consumption of 1/2 cup of blueberries or an equivalent source of flavonoids on a daily basis is likely to have substantial benefits for maintaining cognitive and motor function.

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