EFFECT OF WHOLE FRUIT BASED ANTHOCYANINS ON SYSTEMIC INFLAMMATION, OXIDATIVE STRESS, AND WAIST CIRCUMFERENCE IN WOMEN

By

Anastasiya Yudinova

A Project Presented to

The Faculty of Humboldt State University

In Partial Fulfillment of the Requirements for the Degree

Master of Kinesiology in Exercise Science

Committee Membership

Dr. Taylor Bloedon, Committee Chair

Dr. Rock Braithwaite, Committee Member

Dr. Jill Anderson, Committee Member

Dr. Kari Pilolla, Committee Member

Dr. Taylor Bloedon, Program Graduate Coordinator

December 2021

Abstract

EFFECT OF WHOLE FRUIT BASED ANTHOCYANINS ON SYSTEMIC INFLAMMATION, OXIDATIVE STRESS, AND WAIST CIRCUMFERENCE IN WOMEN

Anastasiya Yudinova

Cardiometabolic disease (CMD) remains the leading cause of death nationally. Intra-abdominal fat (IAF) is one of the primary risk factors for CMD. Women are particularly vulnerable to developing CMD due to hormonal changes during and after menopause that increase IAF. Excess IAF has deleterious effects on the body, increasing systemic inflammation and oxidative stress, leading to CMD. This systematic review and meta-analyses examined current research related to consumption of whole foods high in anthocyanins, their impact on oxidative stress and inflammation, and the medium and amount of anthocyanin delivery that yields the most benefits to women at risk for CMD. This meta-analysis included 47 studies extracted using PRISMA 2020 guidelines. Overall, effect sizes were not significant when exploring obesity, inflammation, and oxidative stress outcomes. Subgroup analyses did yield some significant results, however, small reporting values and large heterogeneity statistics rendered most outcome effect sizes unreliable. Future research should consider standardizing anthocyanin treatment protocols to allow readers to draw conclusions and make research-based recommendations more easily.

Acknowledgements

A low bow goes to Dr. Braithwaite and Dr. Bloedon for staying by me through this entire project. You helped and taught me so much. I could not have done this without your expert guidance.

Table of Contents

List of Tables

List of Figures

Introduction

Cardiometabolic diseases (CMD), which includes diseases such as type 2 diabetes and cardiovascular (CVD) disease, have been associated with growing healthcare costs in the U.S for decades. In 2019, a total of 2.7 trillion dollars was spent on all CVD-related care (Institute for Health Metrics and Evaluation, 2019b). The same year, the same amount was spent on care for diabetes, with the largest portion (46.31%) spent on prescribed pharmaceuticals. Having a cardiometabolic condition, can more than double one's personal medical expenses, reduce job productivity, and increase disability-associated time off (Economic Costs of Diabetes in the U.S. in 2017, 2018). Collectively, heart disease, diabetes mellitus, hypertension, stroke, and obesity were responsible for over 4.8 million deaths within the U.S. population of those ages 25-64 between the years of 1990 and 2017 (Harris, Majmundar, and Becker, 2021, p. 311). The Centers for Disease Control and Prevention (CDC) reported that heart disease remains the leading cause of death nationally, killing 655,381 people in 2018 (National Center for Health Statistics, 2021, Table 006). According to the Institute for Health Metrics and Evaluation's Global Burden of Disease Data (2019a), high body mass index (BMI) represents the leading risk factor for CVD and contributes to 6.8% of deaths among the population 15-49 years of age in the U.S., followed by high blood pressure (6.49%). These rates increase for those ages 50-69, 10.85% and 12.97%, respectively. However, there are co-contributing factors to the development of CMD, many of which occur simultaneously (Kahn et al, 2005), such as age, genetics, family history, inflammation,

hypertension, smoking, physical inactivity, unhealthy diet, hyperlipidemia, insulin resistance, reduced quality of life, and obesity (Brunzell et al, 2008, Fig. 1).

Obesity is a risk factor for metabolic syndrome (MetS), a precursor to CMD (Grundy et al, 2004; Dragsbæk et al, 2016), includes symptoms such as hyperlipidemia, hyperglycemia, and hypertension (Expert Panel on Detection, Evaluation, And Treatment Of High Blood Cholesterol In Adults (ATP III), 2001). There are many factors that contribute to obesity such as race and ethnicity, education and income levels, higher cost of healthier foods (Finkelstein et al, 2012), smoking, lower vegetable and fruit consumption, physical activity level (Bonauto, Lu, & Fan, 2014), alcohol consumption (Baik & Shin, 2008), low sleep duration (Gangwisch et al, 2005), and psychological distress (Brandheim, Rantakeisu, & Starrin, 2013). Many of the same factors are also considered risks for developing CMD according to ATP III (2001) and Dragsbæk et al (2016). However, studies show that, in particular, intra-abdominal fat (IAF) correlates with MetS (Grundy et al, 2004; Dasgupta et al, 2012) and independently increases the risk for CVD and diabetes by a factor of 1.5 and 2, respectively (Dragsbæk et al, 2016). The ATP III (2001) lists excess IAF as one of the primary metabolic risk factors used to predict cardiometabolic conditions such as stroke, diabetes, and heart disease. Researchers found that waist circumference (WC), an indicator of IAF status, correlates with various CMD risks (Browning, Hsieh, & Ashwell, 2010; Codoñer-Franch et al, 2012; Dasgupta et al, 2012). The World Health Organization reports that WC measurements ≥ 80 cm (~32 inches) indicates an increased risk for metabolic complications, while ≥ 88 cm (~35 inches) substantially increases those risks for

Caucasian women (Obesity: preventing and managing the global epidemic., 1999, Table 2.2). While the aforementioned WC cut-off values may be sufficient indicators for Caucasian women when used for early detection, more research is needed to determine cut-off values for other racial and ethnic groups.

Much effort has been applied to understanding the exact factors which lead to an increase in IAF, particularly for those of menopausal age (Razmjou et al, 2018).While aging is related to increases in body weight (Ambikairajah et al, 2019), mainly due to a decline in basal metabolic rate (BMR) and physical activity (Dasgupta et al, 2012; Razmjou et al, 2018), weight gain has not been shown to have an independent, positive relationship with IAF accumulation and fat distribution (Dasgupta et al, 2012; Ambikairajah et al, 2019). However, significantly higher WC values were reported in postmenopausal women after adjusting for normal aging (Kim et al, 2007). Based on hormone replacement therapy (HRT) outcome measurements, other studies suggest that changes in sex hormones during menopause influence IAF accumulation and associated MetS risk factors (Goss et al, 2012; Perry et al, 2013; Lizcano & Guzman, 2014; Razmjou et al, 2018; Ambikairajah et al, 2019). Once the ovaries cease to make estrogen, adipose tissue becomes the primary source of estrogens (estrone and estradiol), higher levels of which can be found in obese women (Liedtke et al, 2012; Stefanska, Bergmann, and Sypnietwska, 2015), linking menopausal transition to central obesity. Research also shows that the decrease in sex hormone–binding globulin (SHBG) during menopause is connected to the increase in free testosterone (free T) (Ziaei and Mohseni, 2013; Stefanska, Bergmann, and Sypnietwska, 2015). A relationship between free T levels and

IAF accumulation, independent of age or estrogen, was confirmed in a longitudinal study of 102 Australian women at varying stages of menopause (Guthrie et al, 2003), while SHBG has been found to have a relationship with all aspects of MetS (Weinberg et al, 2006; Ziaei and Mohseni, 2013). A cross-sectional analysis of 1180 postmenopausal German women found correlations between WC, estrogen, free T, and SHBG (Liedtke et al, 2012). Menopausal transition seems to bear influence on body fat distribution (Razmjou et al, 2018), making women more vulnerable than men to increasing central obesity or IAF accumulation with age. In a randomized, double-blind, placebo-controlled study, 51% of 212 participants not undergoing HRT met the criteria for metabolic syndrome (Weinberg et al, 2006). Cross-sectional data of 358 Brazilian participants showed that postmenopausal women were at a 4.88 times higher risk for central obesity than premenopausal women (Donato et al, 2006), further underlying that menopause predisposes women to MetS (Ziaei and Mohseni, 2013; Sapkota et al, 2015). An increased accumulation of IAF puts women at a higher risk for CMD, particularly the case for black women during pre and perimenopausal phases, reported by Gurka et al, (2016).

Reducing the amount of IAF in the body is an important health measure for decreased risk of cardiometabolic diseases through the reduction of inflammation causing pathways associated with IAF. Adipose tissue is not only a form of excess energy storage but is also an established endocrine organ (Zhang et al, 1994; Jung & Choi, 2014). Adipocytes secrete adipokines or adipocytokines, many of which are involved in inflammation (Jung & Choi, 2014; Stefanska, Bergmann, and Sypnietwska, 2015) such as

TNFα, leptin, and interleukins (IL) (Kershaw & Flier, 2004). Most of the pro-inflammatory cytokines, like TNFα, are made by M2-polarized macrophages within adipocytes (Lee et al, 2014), the content of which is positively related to adipocyte size (Weisberg et al, 2003) and IAF gain. The increase in pro-inflammatory cytokines causes an influx of reactive oxygen species (ROS), by-products of oxygen metabolism, which, under normal conditions, would be neutralized by the body to maintain equilibrium (Bahoran et al, 2007; Pham-Huy, He, and Pham-Huy, 2008). ROS adversely affect other molecules, such as lipids, proteins, and nucleic acids in the body, causing oxidative stress (OS) (Bahoran et al, 2007; Pham-Huy, He, and Pham-Huy, 2008), which has been shown to lead to insulin resistance and other CMD risk factors (Abella et al, 2014; Paneni, Costantino, and Cosentino, 2015). This relationship between IAF, OS, and inflammation has been observed by multiple studies (Codoñer-Franch et al, 2012; Emanuela et al, 2012; Jung and Choi, 2014; Abbasian et al, 2018; Jia et al, 2019).

Lifestyle changes, such as eating a plant-based diet, have shown to be effective at reducing weight and cardiometabolic risks (Trapp and Levin, 2012), along with the potential to reduce the number of prescribed medications (Tuso et al, 2013) and associated costs. Jardim et al (2019) reported a national total of $50.4 billion in CMD-related annual costs due to a suboptimal diet. Consuming an optimal number of fruits (300g/day) and vegetables (400g/day) alone could reduce the national annual CMD medical costs by $9.55 billion and $10.06 billion, respectively (Jardim et al, 2019). Particularly polyphenol-rich plant foods have shown beneficial effects on cardiovascular health (Grosso et al, 2016; Mendonça et al, 2019). Polyphenols, a type of organic

bioactive compounds, are strong antioxidants (Scalbert and Williamson, 2000), which have the capacity to locate and neutralize free radicals or ROS (Halliwell, 1997) and are of particular interest in the search for less costly, natural preventative health alternatives. In particular, polyphenols increase antioxidant enzyme activity, reduce lipid peroxidation, directly scavenge free radicals (Nakagawa and Yokozawa, 2002), and reduce oxidation by chelating or binding metal ions (Yiannakopoulou, 2013). Polyphenols react with ROS to form more stable molecules, thus removing free radicals. By chelating transition metals, such as calcium (Guo, Bezard, and Zhao, 2005), and increasing antioxidant enzyme activity in the body, polyphenols like anthocyanins can prevent the production of free radicals in the first place (Yan et al, 2020). A study examining 8821 Polish adults found that those individuals in the upper quartile for total polyphenol consumption (specific foods were not mentioned) had a significantly lower value associated with WC, triglycerides, blood pressure, and were less likely to develop MetS (Grosso et al, 2016). Other studies indicate that red, purple, and blue-colored foods containing high amounts of anthocyanins, a type of polyphenol, expressed in the plant's color (Strack and Wray, 1993), have shown significant effects on inflammation and OS (Bloedon et al, 2019). For example, Tulipani et al (2011) found that the daily consumption of 500g of fresh strawberries for 16 days significantly increased plasma vitamin-C levels and contributed to increasing human erythrocyte resistance to oxidation. Moazen et al (2013) used 2 cups equivalent of daily freeze-dried strawberry juice and reported a significant decrease in inflammation and lipid peroxidation, along with an increase in total antioxidant capacity (TAC) after 6 weeks. A randomized clinical trial by Sohrab et al (2016) confirmed that

200ml of fresh pomegranate juice (PJ) daily for 6 weeks significantly decreased oxidized and anti-oxidized LDL antibodies, while increasing the TAC of their participants, contributing to positive effects on OS. Similarly, Shishehbor et al (2016), also examined (PJ) benefits, and found a significant reduction in serum interleukin-6 and a substantial increase to TAC in 4 weeks of daily PJ concentrate consumption of only 50g. In the previous examples, we can note a trend of differences in anthocyanin delivery such as the amount and condition of the food, as well as study duration, and general methods. Additional studies assessing polyphenol benefits on inflammation and OS markers also use varying types of berries such as those by Rahbar, Mahmoudabadi, and Islam (2015), Lynn et al (2014), and Loo et al (2016), who use fresh white grapes, tart cherry juice concentrate, and oven-dried chokeberry powder and fresh juice, respectively. Kolehmainen et al (2012), Johnson et al (2015, 2017), Espinosa-Moncada et al (2018) used bilberry puree and freeze-dried powder, freeze-dried whole blueberries, and freeze-dried whole agraz, respectively. Other variations in berries included using a blend of grape, cherry, blackberry, black currant, and raspberry juice concentrate (Garcia-Alonso et al, 2006), fresh cranberry juice (Dohadwala et al, 2011), and fresh plum juice to supply polyphenols (Bhaswant, Brown, and Mathai, 2019). One study, which looked at the effects of polyphenols on WC, used flash-frozen acai berries (whole and puree) (Barbosa et al, 2016), adding to the extended list of possible anthocyanin-rich food recommendations. Existing research into the effects of anthocyanins reflects a broad range of types of fruits used, food processing methods, intake quantities, and intervention timelines, making it difficult to draw usable conclusions for recommendations. This

meta-analysis aimed to examine current research related to consumption of whole foods high in anthocyanins, their impact on OS and inflammation, and the medium and amount of anthocyanin delivery that yields the most benefits to women at risk for CMD.

Methods

Study Design

This systematic review meta-analysis investigated the effect of whole fruit-based anthocyanins on inflammation and OS markers, as well as WC in women. Recently published peer-reviewed articles were simultaneously screened by two researchers, following strict guidelines. The search was conducted through the California State University library interface focusing on three databases and one register: ScienceDirect, PubMed, WebOfScience, and ProQuest. This systematic review followed the PRISMA 2020 screening process recommendations, which can be accessed at http://www.prisma-statement.org/.

Search Protocol

The initial phase, performed by two junior researchers, consisted of using the advanced search feature within each database and limiting the articles to those with human subjects, written in English, and published in the year 2000 or later. To further narrow down the search results, search terms directly related to CMD and polyphenols were added. See Table 1 for a detailed list of terms used. Each polyphenol-related search term was combined with a study-related search term to yield a total of 96 combinations per database. Articles titles were subsequently screened for relevance and added to one of three folders: “Yes” folder (relevant), “No” folder (irrelevant), and “Maybe” folder (possibly relevant). Each article deemed relevant based on its title was also saved to EndNote, a citation managing software. All duplicate entries were deleted. In the second phase, two senior researchers performed all of the following steps to reduce the

possibility of exclusion error. The “Yes” and “Maybe” articles were screened again based on abstract relevance and further sorted into “Yes” or “No” folders. The third phase consisted of obtaining each remaining article in full text from the associated database or through the Interlibrary Loan system. The full text documents were then screened based on PICOS inclusion/exclusion criteria (see Table 2) and grouped according to those that met all the criteria, did not meet the criteria, or were not clear. The articles that met all the inclusion criteria had to identify an intervention, study the effects of anthocyanins, use whole fruits high in anthocyanins, have female participants, and include quantitative cardiometabolic indices. Those articles that did not meet the criteria were excluded from the meta-analysis, while those that were not clear were reevaluated for inclusion or exclusion by both senior researchers.

Table 1

Article Title Search Terms

Polyphenol-Related	**Study-Related**	
anthocyanin	intervention	diabetes
polyphenol and/or flavonoid	randomized control trial	waist circumference
berry and/or berries	experimental design	central obesity or abdominal obesity
currant	hypertension	glycemic
grape	blood pressure	inflammation
pomegranate	lipid	adipose
	cholesterol	metabolic syndrome
	insulin	cardiometabolic
	glucose	

Table 2

PICOS Inclusion/Exclusion Criteria

Parameter	Inclusion	Exclusion
Participants	Adult women aged 18 – 65 y	< 18 y; no women
Study design	Experimental, quasi-experimental, English language, published from 2000-2021	Supplements with extracts of other fruits or ingredients other than for palatability; non-whole fruit derived anthocyanins
Intervention	Supplementation with whole fruit high in anthocyanins (various processing allowed)	None
Comparison	Placebo or pre-post, same group comparison	Change in non-biological markers
Outcomes	Change in biological oxidative stress and/or inflammatory markers and/or WC	Reviews, abstracts, editorials, non-English language

Note: WC - waist circumference

Data Collection

The next process consisted of specific data collection from the full text documents based on a coding sheet (see simplified version in The Appendix) with three primary categories: participant characteristics, intervention characteristics, and study characteristics. See Table 3 for a list of subcategories. If any of the required information was unclear or missing from the text, such as p-values or standard deviations, the author

of the associated article was contacted via email in an attempt to acquire the missing details. Contact was made three times with a two-week waiting period between each email. If no response was received from an author after 6 weeks, that study was excluded from the sample.

Table 3

Data Collection Categories

Participant Characteristics	**Intervention Characteristics**	**Study Characteristics**
Sex Age Health status Menstrual status Weight category BMI	Subgroup of fruit Time points of marker measures Protocol Fruit name Fruit processing Fruit delivery schedule Fruit Dose Fresh fruit equivalent Total daily anthocyanins (mg) Marker outcomes Experimental/treatment mean Experimental/treatment standard deviation Experimental/treatment number of participants Control group mean Control group number of participants T-value P-value Group comparison Design type Baseline measures Total duration Washout Intervention environment	Author Location Funding status Publishing status

Data Reformatting

All the gathered data according to Table 3 was converted to standardized units where needed and organized into the aforementioned subcategories. Any conversions were

made using the American Medical Association online calculator, which can be found at http://phenol-explorer.eu/.

Fresh fruit value equivalents were collected where available or calculated based on provided data of fresh fruit. The same process was repeated for anthocyanin quantities (see Appendix for actual values), recorded as cyanidin-3-glucoside, and categorized as <50mg, 50-100mg, 100-400mg, >400mg, or comparative (multiple anthocyanin amounts used in the intervention) for subgroup analyses. The age of study participants was recorded using the mean value provided and sorted into groups of either 24-55 or >55 years. Participants' health status was noted as healthy or not, as reported, based on their MetS status, blood lipid status, and blood sugar status. Study duration was noted as stated and categorized into ≤ 2 weeks, 2-8 weeks, and ≥ 8 weeks for subgroup analyses in Table 5 (see Appendix for specific durations). Weight groups were based on the given mean BMI scores in each study: healthy (18-24.9), combined (>18), overweight (25-29.9), overweight combined (18-29.9), obese (30-34.9), obese combined (18-34.9).

Statistical Analyses

The software used for all the statistical analyses was Comprehensive Meta-Analysis Version 2 Software (CMAv.2). The first step of the process was to check our sample for outliers. Outliers were defined as any study with a residual value of 1.96 standard deviations below or above the overall mean effect. If an outlier existed, a sensitivity analysis was used to determine the influence of that particular study on the rest of the data. If the data was no longer significant after the outlier was removed, the outlier would be left out. If the data remained significant within the 95% confidence interval, the outlier was

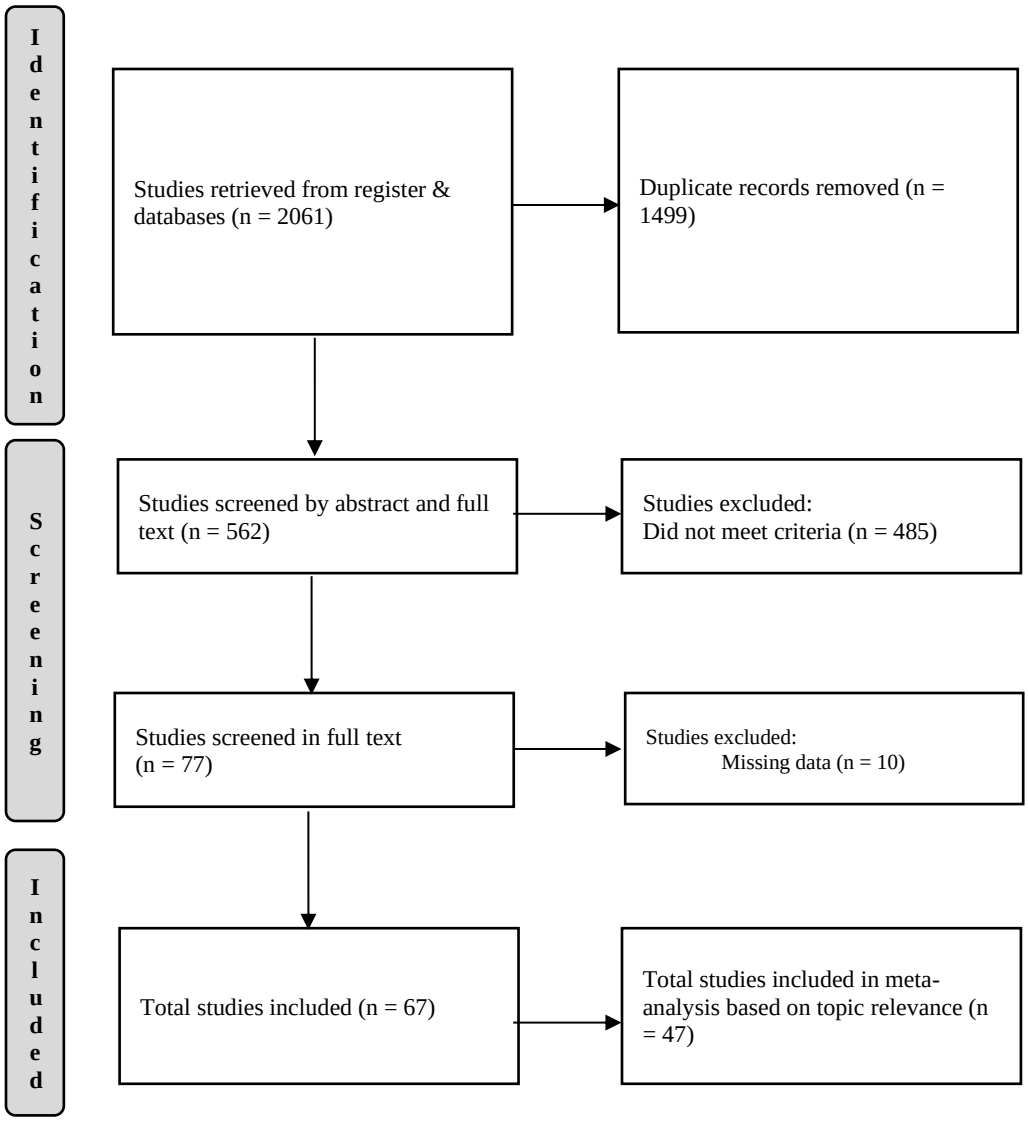
kept as part of the sample. Next, publication bias was assessed using 3 methods: the funnel plot, the trim and fill procedure, and the file drawer analysis (fail safe N). Using the funnel plot required assessing whether the data distribution is symmetrical. If it is, there is no bias. If the data is not symmetrical, then publication bias exists in the sample and a trim and fill procedure is necessary. This procedure mathematically estimates the number and location of studies that would be needed within the existing sample in order to balance the funnel plot distribution and create symmetry. The file drawer analysis or "fail safe N" helps assess how many studies with nonsignificant results would have been missed to nullify the results in this meta-analysis. To evaluate the effect size of subgroups smaller in size than 20, Hedge's g metric was used. Since this meta-analysis included studies with varying samples and methods, the random effects model was chosen to interpret the errors associated with our heterogeneous sample. There are three ways that heterogeneity of variance is assessed: Q-value, t^2- value, and the I^2-value. The Q-value is an estimate of how different the studies in the sample were and whether that value is significant ($\leq .05$). The t^2 - value indicates the size of the between-study variance from 0 - 1.0, with larger numbers meaning more variability. Finally, the I^2-value reports the amount of true heterogeneity that can be explained with the subgroup analysis such as small 25% ($I^2 = 25$), medium 50% ($I^2 = 50$), and large 75% ($I^2 = 75$) (Higgins and Thompson, 2002).

Results

The purpose of this study was to determine the most effective medium and amount of whole foods high in anthocyanins to consume in order to mitigate the impacts of inflammation and oxidative stress in women. A total of sixty-seven studies met the inclusion criteria after the third phase of screening. Figure 1 displays the overall screening process. During that process, twelve studies were missing the necessary information. One author failed to provide the necessary information, while nine did not respond. There were no researcher disagreements for the final set. Out of the sixty-seven accepted studies, 47 were chosen for this meta-analysis based on topic relevance related to inflammation, oxidative stress, and waist circumference.

Figure 1

Search Strategy and Article Screening Process



Random Effects Model

Cohen's categorization system was used to interpret treatment effect sizes with ≥ .20 being small, ≥ .05 being medium, and ≥ .80 being large (Cohen, 1988). The overall

treatment effect for all the studies within the sample was small and not statistically significant across all outcomes (g = .10; SE = .10; 95% $C.I.$ = -.09, .29; p = .32). A moderator or subgroup analysis was conducted on all coded characteristics to better explain the between-study variance. Only one subgroup analysis, the study design subgroup, yielded a significant heterogeneity value (Q = 9.12, df = 3, p = .03).

Outliers

Four studies within our sample were found to be outliers based on their z-scores: Asgary et al. (2014) (z = 3.08), Aviram et al. (2004) (z = 5.73), Boldaji et al. (2019) (z = 5.06), and Rahbar et al. (2015) (z = -8.95). A sensitivity analysis was performed for each outlier via the "one study removed" procedure and determined changes to the statistical model if removed. All studies were retained as overall results remained similar ($\pm$ 0.12) and within the 95% confidence interval.

Publication Bias

All outcome categories in Table 4 were assessed for publication bias and reported with the "fail safe N" value. The funnel plot had a symmetrical distribution and a trim-and-fill procedure was not necessary. The fail-safe procedure yielded zero values (N = 0) for the majority of the outcome subcategories. If these categories were reported by at least 10 studies, a zero value of N would suggest possible presence of bias if no studies were needed to nullify significant results. However, most of the subcategories of inflammation outcomes and antioxidant capacity outcomes were reported by too few studies to make determinations on bias or effect size reliability. Within inflammation outcomes, C-reactive protein (CRP) (N = 140), and Interleukins (IL) (N = 0) were the

only ones reported by more than 10 studies. CRP N-value suggests that publication bias is unlikely while IL N-value may suggest the presence of bias. Within the antioxidant capacity outcomes, none of the subcategories were reported by enough studies to speak on possible bias with any certainty. Waist circumference yielded a fail-safe N value of zero, while also having been reported by over 10 studies ($k = 13$), indicating possible presence of publication bias.

Outcome Analyses

Outcome analyses in Table 4 produced both positive and negative effects, ranging from $g = -.00$ to $g = 1.50$. Outcome groups with positive effect values included C-reactive protein, interleukins, malondialdehyde, FRAP, nitric oxide, and paraoxonase 1. For groups with at least five studies ($k \geq 5$) the largest positive effects, all non - significant, were produced by C-reactive protein ($k = 25$, $g = .21$, $p = .11$) and nitric oxide ($k = 5$, $g = .90$, $p = .13$). Outcome groups with negative values included adiponectin, leptin, oxidized LDL, sICAM 1, sVCAM 1, TNFa, ORAC, superoxide dismutase, total antioxidant capacity, and waist circumference. Out of these, groups with five or more studies that showed at least a low effect size ($g \geq -.20$) were sVCAM 1 ($k = 6$, $g = -.20$, $p = .57$), TNFa ($k = 9$, $g = -.24$, $p = .37$), and total antioxidant capacity ($k = 7$, $g = -.33$, $p = .42$), also all not statistically significant.

Moderator Analyses

Results for the random effects model confirmed existing heterogeneity in the sample distribution ($Q = 248.52$, $p = .32$) and that a large portion of between-study variance could be explained by conducting a subgroup analysis ($I^2 = 81.49$) in Table 5.

The p-value indicates that the between-study variance was random. The use of subgroup analyses with fewer than five studies ($k < 5$) was purely for discussion purposes as the analysis results for these groups can be less precise (Borenstein et al., 2009).

Sample Characteristics

There were no significant differences between subgroups within sample characteristics, however, several small to medium within-subgroup effects were found. Over 55 years of age group ($k = 14$, $g = .30$, $z = 1.71$, $p = .09$), fruit delivery daily single serving group ($k = 30$, $g = .28$, $z = 2.24$, $p = .03$), fresh juice fruit processing type group ($k = 17$, $g = .47$, $z = 2.68$, $p = .01$), and the post-menopause group ($k = 18$, $g = .22$, $z = 1.39$, $p = .16$) all yielded small effect sizes. Out of these, only the daily single serving and fresh juice groups produced significant ($p \leq .05$) g-values. The BMI overweight group ($k = 7$, $g = .54$, $z = 2.00$, $p = .05$) and pomegranate fruit type groups ($k = 11$, $g = .69$, $z = 2.93$, $p = .00$), both statistically significant ($p \leq .05$), yielded the only medium size effects post within-subgroup analyses. A high degree of heterogeneity was observed among the aforementioned statistically significant sample characteristics indicated by the Q and t^2 values, with potential to explain the between-study variance ($I^2 > 70$).

Table 4

Inflammation, Oxidative Stress, & Waist Circumference Outcome Analyses

	k	*g*	SE	S^2	95% CI	Z	P-value	Q	τ^2	I^2	Fail safe N
Inflammation Outcomes											
Adiponectin	3	-.04	.39	.15	-.81, .73	-.11	.91	8.63*	.35	76.81	0
C-Reactive Protein	25	.21	.13	.02	-.05, .47	1.59	.11	138.28**	.34	82.64	140
Interleukins	12	.13	.11	.01	-.07, .34	1.27	.20	18.17	.05	39.47	0
Leptin	2	-.05	.23	.05	-.50, .41	-.20	.85	.00	.00	.00	0
Malondialdehyde	4	1.44	.94	.89	-.41, 3.29	1.53	.13	62.60**	3.32	95.21	14
Oxidized LDL	7	-.00	.12	.02	-.25, .24	-.03	.98	6.91	.01	13.21	0
sICAM 1	7	-.12	.24	.06	-.58, .35	-.49	.62	20.17*	.27	70.25	0
sVCAM 1	6	-.20	.36	.13	-.90, .49	-.58	.57	28.67**	.61	82.56	0
TNFa	9	-.24	.27	.07	-76, .28	-.90	.37	59.86**	.54	86.63	0
Antioxidant Capacity Outcomes											
FRAP	6	.06	.14	.02	-.22, .33	.39	.70	7.68	.04	34.89	0
Nitric Oxide	5	.90	.59	.35	-.25, 2.06	1.53	.13	51.59**	1.60	92.25	24
ORAC	1	-.11	.29	.08	-.66, .45	-.37	.71	.00	.00	.00	0
Paraoxonase 1	3	1.50	.79	.63	-.06, 3.05	1.89	.06	43.01**	1.60	95.35	21
Superoxide Dismutase	3	-.06	.19	.04	-.43, .32	-.30	.77	2.28	.01	12.15	0
Total Antioxidant Capacity	7	-.33	.41	.17	-1.13, .47	-.81	.42	101.74**	1.08	94.10	0
Obesity											
Waist Circumference	13	-.03	.09	.01	-.21, .15	-.30	.77	14.85	.02	19.19	0

CI confidence intervals (lower limit, upper limit), g effect size (Hedges' g), I^2 total variance explained by moderator, *k* number of effect sizes, S^2 variance, *SE* standard error, *Z* test of null hypothesis, *p < 0.05, ** p < 0.001, *Q* used to determine heterogeneity, τ^2 indicates between study variance in random effects model, *Interleukins* (1b, 6, 8, 10, 18), *FRAP* ferric reducing ability of plasma, *ORAC* oxygen radical absorbance capacity, *Oxidized LDL* low-density lipoproteins, *sICAM 1* soluble intercellular adhesion molecule-1, *sVCAM 1* soluble vascular cell adhesion molecule-1, *TNFa* tumor necrosis factor alpha.

Intervention Characteristics

Study design was the only intervention characteristic to produce significant differences between subgroups. Crossover study design (k = 12, g = .30, z = 1.58, p = .11), study duration less than or equal to 2 weeks (k = 5, g = .43, z = 1.33, p = .18), and studies with a washout period equal to or over 2 weeks (k = 9, g = .44, z = 1.94, p = .05) showed small within-subgroup differences, none statistically significant.

Study Characteristics

None of the three subgroups showed between-groups differences. Unfunded studies produced the only non-significant small within-groups effect size (k = 11, g = .25, z = 1.23, p = .22).

Table 5

Moderators Subgroup Analyses

	k	***g***	**SE**	S^2	**95% CI**	**Z**	**P-value**	**Q**	τ^2	I^2
Sample Characteristics[B]										
Random Effects[A]	**47**	**.10**	**.10**	**.01**	**-.09, .29**	**.99**	**.32**	**248.52**	**.34**	**81.49**
Age								**1.92 [B]**		
24-55	33	.01	.12	.01	-.22, .23	.07	.94	151.51**	.30	78.88
>55	14	.30	.17	.03	-.04, .64	1.71	.09	80.02**	.37	83.75
BMI								**4.72 [B]**		
Healthy	5	.10	.30	.09	-.49, .69	.34	.74	3.97	.00	.00
Overweight	7	.54	.27	.07	.01, 1.07	2.00	.05*	44.50**	.51	86.52
Overweight combined	14	.00	.19	.04	-.37, .37	.00	1.00	139.22**	.82	90.66
Obese	6	-.16	.29	.08	-.72, .41	-.54	.59	5.08	.00	1.57
Combined	12	.19	.20	.04	-.21, .58	.92	.36	31.20**	.16	64.75
Not reported	3	-.26	.39	.15	-1.03, .51	-.66	.51	9.34*	.27	78.72
Menstruation								**1.20 [B]**		
Mixed	27	.00	.13	.02	-.25, .26	.03	.98	138.21**	.33	81.19
Post-menopause	18	.22	.16	.03	-.09, .53	1.39	.16	96.46**	.37	82.38
Pre-menopause	2	.23	.46	.21	-.67,	.49	.62	.89	.00	.00

	k	*g*	SE	S^2	95% CI	Z	P-value	Q	τ^2	I^2
					1.12					
Sex								**.01** [B]		
Female	10	.08	.21	.04	-.33, .49	.38	.71	17.38*	.07	48.22
Male & Female	37	.10	.11	.01	-.12, .32	.92	.36	230.37**	.43	84.37
Intervention Characteristics[B]										
Random Effects [A]	**47**	**.10**	**.10**	**.01**	**-.09, .29**	**.99**	**.32**	**248.52**	**.34**	**81.49**
Anthocyanins								**.62** [B]		
<50	28	.16	.14	.02	-.12, .42	1.16	.25	222.13**	.61	87.85
50-100	3	.16	.38	.15	-.59, .91	.43	.67	4.35	.06	54.03
100-400	12	-.02	.20	.04	-.41, .37	-.10	.92	15.27	.03	27.95
>400	2	.08	.47	.22	-.85, 1.01	.17	.86	2.67	.11	62.61
Comparative	2	.00	.50	.25	-.99, .99	.00	.10	.05	.00	.00
Fruit Delivery								**5.92** [B]		
OT single serving	2	-.06	.49	.24	-1.02, .90	-.12	.91	.00	.00	.00
Daily single serving	30	.28	.13	.02	.04, .53	2.24	.03*	95.11**	.17	69.51
Daily multiple servings	15	-.24	.18	.03	-.58, .11	-1.37	.17	152.68**	.80	90.83
Fruit Processing								**7.53** [B]		
Dried	2	.15	.50	.25	-.83, 1.13	.29	.77	.05	.00	.00
Flash frozen	2	.01	.46	.22	-90, .92	.03	.98	1.18	.01	14.92
Freeze-dried	14	-.12	.19	.04	-.48, .25	-.61	.54	19.21	.05	32.33
Fresh	5	-.27	.31	.09	-87, .33	-.88	.38	100.25**	1.63	96.01
Juice conc	5	.02	.31	.10	-.59, .63	.07	.94	1.03	.00	.00
Juice fresh	17	.47	.18	.03	.13, .82	2.68	.01*	106.81**	.45	85.02
Multiple	2	-.11	.50	.25	-1.08, .86	-.23	.82	.17	.00	.00
Fruit Type								**12.69** [B]		
Acai	1	.17	.68	.46	-1.16, 1.50	.25	.81	.00	.00	.00
Agraz	1	.37	.70	.49	-1.00, 1.74	.53	.60	.00	.00	.00
Bilberry	3	-.20	.42	.18	-1.02, .63	-.47	.64	.05	.00	.00
Blend	1	-.06	.73	.53	-1.49, 1.37	-.08	.93	.00	.00	.00
Blueberry	2	-.49	.52	.27	-1.52, .53	-.94	.35	5.50*	.53	81.83
Cherry, sweet	2	.39	.50	.25	-.59, 1.37	.77	.44	.37	.00	.00
Cherry, tart	4	-.03	.36	.13	-.75, .68	-.09	.93	.70	.00	.00
Choke/Aronia	4	-.01	.35	.12	-.70, .68	-.04	.97	2.12	.00	.00
Cranberry	1	.12	.72	.52	-1.29, 1.54	.17	.86	.00	.00	.00

	k	*g*	SE	S^2	95% CI	Z	P-value	Q	τ^2	I^2
Grape	7	-.42	.28	.08	-.96, .13	-1.49	.14	77.64**	1.22	92.27
Plum	1	.25	.75	.57	-1.23, 1.72	.33	.75	.00	.00	.00
Pomegranate	11	.69	.24	.06	.23, 1.15	2.93	.00*	93.80**	.67	89.34
Strawberry	8	.06	.26	.07	-.46, .57	.21	.83	21.14*	.21	66.89
Wild blueberry	1	.57	.74	.55	-.88, 2.03	.77	.44	.00	.00	.00
Baseline								**.66** [B]		
No	2	.46	.46	.21	-.44, 1.37	1.00	.32	.23	.00	.00
Yes	45	.08	.10	.01	-.12, .28	.80	.43	245.90**	.35	82.11
Study Design								**9.12** [B]*		
Experimental	24	.12	.14	.02	-.15, .39	.87	.39	113.87**	.31	79.80
Parallel	4	-.88	.35	.12	-1.56, -.20	-2.53	.01*	66.89**	3.15	95.52
Quasi-experimental	7	.16	.24	.06	-.30, .63	.69	.49	6.76	.01	11.21
Crossover	12	.30	.19	.04	-.07, .68	1.58	.11	40.45**	.23	72.81
Study Duration								**1.67** [B]		
≤ 2 weeks	5	.43	.32	.11	-.20, 1.07	1.33	.18	11.48*	.22	65.16
2-8 weeks	22	.13	.14	.02	-.15, .41	.93	.36	25.87	.02	18.84
≥ 8 weeks	20	-.02	.16	.02	-33, .29	-.12	.90	210.52**	.85	90.98
Washout Period								**2.82**		
< 2 weeks	6	.06	.27	.07	-.47, .58	.21	.84	6.64	.02	24.64
≥ 2 weeks	9	.44	.23	.05	-.01, .89	1.94	.05	31.12**	.30	74.29
No washout	32	.01	.12	.01	-.23, .25	.09	.93	204.71**	.41	84.86
Study Characteristics[B]										
Random Effects [A]	**47**	**.10**	**.10**	**.01**	**-.09, .29**	**.99**	**.32**	**248.52**	**.34**	**81.49**
Funding								**2.52** [B]		
Funded	25	.15	.13	.02	-.11, .41	1.10	.27	52.51**	.10	54.30
Unfunded	11	.25	.20	.04	-.15, .64	1.23	.22	53.38**	.24	81.27
Not reported	11	-.19	.21	.04	-60, .22	-.89	.37	127.96**	1.31	92.19
Location								**25.66** [B]		
Australia	2	.26	.53	.28	-.78, 1.30	.49	.63	.00	.00	.00
Brazil	1	.17	.69	.48	-1.19, 1.53	.24	.81	.00	.00	.00
Canada	1	1.04	.73	.53	-.39, 2.47	1.42	.16	.00	.00	.00
China	1	.13	.78	.60	-1.39, 1.65	.17	.87	.00	.00	.00
Colombia	1	.37	.71	.51	-1.03, 1.77	.52	.60	.00	.00	.00
Finland	2	-.12	.53	.28	-1.15, .92	-.22	.83	.17	.00	.00
Greece	2	.15	.53	.28	-.90,	.28	.78	.05	.00	.00

	k	*g*	SE	S^2	95% CI	Z	P-value	Q	τ^2	I^2
					1.19					
Iran	8	-.01	.28	.08	-.55, .54	-.03	.98	117.14**	1.58	94.02
Israel	1	6.00	1.25	1.55	3.56, 8.44	4.82	.00**	.00	.00	.00
Italy	1	.42	.73	.54	-1.02, 1.86	.57	.57	.00	.00	.00
Poland	1	-.11	.69	.48	-1.48, 1.25	-.17	.87	.00	.00	.00
Portugal	1	-.15	.72	.51	-1.56, 1.25	-.21	.83	.00	.00	.00
Serbia	4	.13	.37	.14	-.60, .85	.34	.73	4.11	.03	26.97
Spain	1	-.06	.74	.55	-1.52, 1.39	-.08	.94	.00	.00	.00
Sweden	1	-.23	.73	.53	-1.66, 1.21	-.31	.76	.00	.00	.00
UK	3	-.03	.44	.19	-.88, .83	-.07	.95	.96	.00	.00
USA	16	.01	.19	.04	-.36, .37	.04	.97	65.89**	.27	77.24
Publication Status								**.00**		
Not published	2	.10	.47	.22	-.83, 1.02	.21	.84	.01	.00	.00
Published	45	.10	.10	.01	-.10, .30	.97	.33	248.45**	.35	82.29

CI confidence intervals (lower limit, upper limit), g effect size (Hedges' g), I^2 total variance explained by moderator, *k* number of effect sizes, S^2 variance, *SE* standard error, *Z* test of null hypothesis, *p < .05, ** p < .001, *Q* used to determine heterogeneity, τ^2 indicates between study variance in random effects model. A = Total *Q*-value used to determine heterogeneity. B = Between *Q*-value used to determine differences between category subgroups ($p < 0.05$), Anthocyanins in mg/day, BMI body mass index, *Overweight combined* mixed BMI group with primarily overweight subjects, *Combined* mixed BMI group, *OT single serving* one-time single serving, *Blend* (grape, cherry, blackberry, black currant, and raspberry juice concentrates), *juice conc* juice concentrate

Discussion

This systematic review and meta-analysis aimed to examine existing literature related to the effects of anthocyanins to extract the most effective whole-food anthocyanin source, processing style, and delivery method for future recommendations aimed at reducing inflammation and oxidative stress associated with abdominal obesity in women. Specific focus was around determining the type of fruit or berry that yields the most antioxidative benefits, what form that fruit should be consumed in (e.g. dried, fresh, frozen, etc.), how many times per day, and in what quantities (mg of anthocyanins).

Inflammation

Inflammation, Oxidative Stress, & Waist Circumference Outcome Analysis (Table 4) did not yield any significant ($p \leq .05$) results. The most reported biomarker of all ($k = 25$) out of our sample of 47 studies was c-reactive protein (CRP). While no statistical significance ($p = .11$) was found, there was a small effect size ($g = .21$). With five out of 25 studies revealing significant results between pre- and post-treatment measurements of CRP (Kelley et al., 2013; Moazzen et al., 2013; Asgary et al., 2014; Moazzen et al., 2017; Chai et al., 2019). Out of all the 25 studies, only one by Davidson et al. (2009) used 146 participants in their treatment group, whereas the rest had 37 or fewer participants per group. CRP is a common and reliable biomarker to use for assessing inflammation and is a strong independent predictor of CVD (Ridker et al., 2002; Sproston and Ashworth, 2018). Larger study samples may be necessary to explore CRP outcomes with more certainty. Much like CRP, malondialdehyde (MDA) showed no significant changes following intervention ($p = .13$) although it did have a large effect

size (g = 1.44). Unfortunately, due to the small number of studies (k = 4) reporting on this outcome, the result of the analysis is not dependable. The high g-value shown in Table 4, however, may merit future research on MDA as an indicator of inflammation. MDA has been generally accepted as a commonly measured biomarker of lipid peroxidation (Khoubnasabjafari et al., 2015; Tsikas, 2017), though there may be complications regarding measurement reliability related to MDA reactivity (Khoubnasabjafari et al., 2015) as well as fluid or plasma storage conditions and duration prior to analysis (Tsikas, 2017). This may have led to the low reporting rate reflected in our meta-analysis. Seven out of nine of the inflammation biomarkers we analyzed were reported by less than ten studies, making it difficult to speak to their effects, even if they turned out statistically significant.

Total Antioxidant Capacity

Antioxidant capacity of whole-fruit anthocyanins was explored as a mitigating factor of oxidative stress. The analysis of associated categories (Table 4) did not yield any significant results. There was a similar issue of low reporting rates for this group of biomarkers (k = 1 - 7), which puts into question the validity of their effect sizes. However, two outcomes worth noting with high effect sizes, approaching alpha-level significance, were nitric oxide (k = 5, g = .90, p = .13) and paraoxonase 1 (k = 3, g = .1.50, p = .06). Nitric oxide is a compound that was first identified as a vasodilator of smooth muscle (Bassenge and Busse, 1988). The studies in our sample investigated this biomarker for its capacity to reduce blood pressure associated with systemic inflammation (Johnson et al., 2015; Kanellos et al., 2017; Stote et al., 2017; Feresin et al.,

2017; Chai et al., 2019). Nitric oxide bioavailability is reduced by its interaction with and overproduction of ROS (Moncada, 2006), therefore it appears to be a reliable indicator of the presence of oxidative stress. Just as with MDA, more studies are needed to explore the relationship of this biomarker with antioxidant capacity of anthocyanin-rich foods. Similarly, paraoxonase 1, an enzyme that protects lipids from oxidation and hydrolyzes peroxides or ROS (Litvinov et al., 2012, Table 1) was only reported by three studies. The reasons for this decision by the majority of this sample's studies is unknown. The very near significant and high effect value (g = .1.50, p = .06) resulting from our meta-analyses warrants future research on this outcome.

Overview of Moderator Analyses

Results from the Inflammation Moderators Subgroup Analysis in Table 5 was the main source for drawing recommendations regarding anthocyanin delivery. Based on the outcome data, it is unclear what amount of daily anthocyanin intake in mg would lead to the most health benefits, as there was no significance or effect worth noting to any of the dosages reported. However, analysis indicated that a daily single serving may be an effective delivery schedule option (k = 30, g = .28, p = .03). This corresponds to prior research reporting significant reduction in serum LDL levels (Jung et al., 2003; Zhang et al., 2011; Zhu et al., 2013;) and total cholesterol (Jung et al., 2003; Zhang et al., 2011; Bogdanski et al., 2012), as well as an increase in HDL (Bogdanski et al., 2012; Zhu et al., 2013; Curtis et al., 2019) and total antioxidant activity (Bogdanski et al., 2012) after treatments involving daily intake of polyphenol-rich foods for up to 6 months. In fruit selection, pomegranate showed a significant moderate effect (k = 11, g = .69, p = .003),

which may point to it being an effective option for anthocyanin consumption. Care should be taken in interpreting these results into concrete recommendations, however, as the number of studies that have reported on pomegranate effects is still relatively low. All the other types of fruits and berries tested have been reported by too few studies, are not statistically significant, and many show that control groups did better than treatment groups, which may speak to their ineffectiveness as an adequate source of anthocyanins or the method with which they are normally processed for convenient consumption. In all of the studies that used pomegranate, it was administered as fresh juice, which could be the reason for its significant effect as pomegranates are not commonly found in frozen or dried form, for example, unlike strawberries or grapes. The subgroup analysis indicated that, as far as fruit processing, fresh juice may be the more effective choice due to its significant moderate effect (k = 17, g = .47, p = .01). No other processing methods (see Table 5) came close to statistical significance or similar effect size. Though there is no significant difference in how anthocyanin treatments affect females versus males, results point to post-menopausal women (k = 18, g = .22, p = .16) over the age of 55 (k = 14, g = .30, p = .09) experiencing antioxidant-related health benefits, though not quite reaching significance. The overweight group analysis yielded significant results and a moderate effect size (k = 7, g = .54, p = .05), however, these values should be interpreted with caution due to the low number of studies reporting on this BMI-level population.

Limitations

The outcome of this systematic review and meta-analyses demonstrates high levels of variability present in this study sample, which likely impacted the results once

studies were clustered. The Simplified Study Coding Sheet (Appendix) reflects these between-study differences. When assessing the effect size (Hedge's g) for each study independently, five studies out of 34 that reported on inflammation outcomes yielded positive, statistically significant results: Kelley et al., 2013 (g = .50, p = .04); Jenkins et al., 2008 (g = 1.04, p = .000); Davidson et al., 2009 (g = 1.30, p = .000); Boldagi et al., 2019 (g = 2.99, p = .000); Asgary et al., 2014 (g = 3.24, p = .002). Out of 21 studies that reported on antioxidant capacity outcomes, only six showed positive, significant effect sizes: Shishehbor et al., 2016 (g = .64, p = .001); Davidson et al., 2009 (g = 1.30, p = .000); Sohrab et al., 2015 (g = .75, p = .02); Kanellos et al., 2017 (g = 2.03, p = .000); Stote et al., 2017 (g = 2.94, p = .000); Aviram et al., 2004 (g = 6.00, p = .000). When looking at the aforementioned ten studies in more detail (Appendix), differences in research protocols can be seen in every category. The preferred study design in these 10 studies was experimental, followed by crossover and quasi-experimental. Study durations lasted anywhere from 1 week to 36 months, with a 4-week timeline chosen by four studies and the rest each being different. Varied timelines can make it difficult to accurately assess certain time-sensitive biomarkers. An example of this can be seen in the studies by Guo et al. (2008) and Sohrab et al. (2015), both of which used 250 ml of fresh pomegranate juice daily, had the same experimental design, but different durations (4 weeks, 12 weeks respectively). Differences in MDA over time can be seen between the changes in treatment group means from baseline to post intervention (-2.32, p < .01 and -1.9, p < .001 respectively), possibly due to the chosen timelines since the number of participants was also similar (n = 13, 22 respectively). The fruit or berry used in the

interventions varied from pomegranate, used by six studies, wild blueberries, strawberries, sweet cherries, and red grapes, each used by one of the remaining studies. Processing methods varied from fresh juice in six cases, juice concentrate in one case, fresh whole puree in two instances, and dried. The daily anthocyanin equivalent given to participants also greatly varied (2.05 - 314 mg/day) due to the specific fruit dosage and number of daily servings chosen by each study (refer to The Appendix). These variations in anthocyanin quantities make it difficult to draw useful conclusions about daily dose and fruit type effectiveness. Major between-study differences were also seen in regards to participants, with the study by Aviram et al., (2004) having the fewest participant in both treatment and control groups (n = 10, 10), followed by Asgary et al., (2014) (n = 11, 10 respectively), second to last study being by Boldagi et al., 2019 (n = 41, 41), ending with a drastic change in treatment and control participants by Davidson et al. (2009) (n = 146, 143 respectively). It is well known that smaller sample sizes, such as up to 30, make accurate analyses and results more challenging to acquire. In addition to variations in participation, studies recruited people of different ages (24-55, >55), with sometimes none or differing health conditions (based on status of MetS, blood lipds, and blood sugar), with varying weight categories (healthy, overweight, obese), and at different stages of menopause (pre-menopasual, post-menopausal, or mix). Based on these dissimilarities, it is difficult to extrapolate what age groups of women, with what health conditions and weight categories, will most benefit from anthocyanin consumption. Future researchers should consider performing repeat studies, using protocols already in existence with, perhaps, small changes, so that comparisons can be made more easily.

More research on the effects of anthocyanins on women's health in general should lead to clearer results in future meta-analyses on the subject of inflammation, oxidative stress, and waist circumference.

Conclusion

This systematic review and meta-analyses examined the effects of whole foods rich in anthocyanins on waist circumference, inflammation, and oxidative stress markers in women. Effect size statistics did not yield any significant results when exploring obesity, inflammation, and oxidative stress outcomes. Small reporting values and large heterogeneity statistics rendered most outcome effect sizes unreliable. Future research should consider standardizing anthocyanin treatment protocols to allow readers to draw conclusions and make research-based recommendations more attainable.

References

Abbasian, M., Delvarianzadeh, M., Ebrahimi, H., Khosravi, F., & Nourozi, P. (2018). Relationship between serum levels of oxidative stress and metabolic syndrome components. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 12*(4), 497-500. doi:10.1016/j.dsx.2018.03.015

Abella, V., Scotece, M., Conde, J., López, V., Lazzaro, V., Pino, J., . . . Gualillo, O. (2014). Adipokines, Metabolic Syndrome and Rheumatic Diseases. *Journal of Immunology Research, 2014*, 1-14. doi:10.1155/2014/343746

Ambikairajah, A., Walsh, E., Tabatabaei-Jafari, H., & Cherbuin, N. (2019). Fat mass changes during menopause: A metaanalysis. *American Journal of Obstetrics and Gynecology, 221*(5). doi:10.1016/j.ajog.2019.04.023

Baik, I., & Shin, C. (2008). Prospective study of alcohol consumption and metabolic syndrome. *The American Journal of Clinical Nutrition, 87*(5), 1455-1463. doi:10.1093/ajcn/87.5.1455

Barbosa, P. O., Pala, D., Silva, C. T., Souza, M. O., Amaral, J. F., Vieira, R. A., . . . Freitas, R. N. (2016). Açai (Euterpe oleracea Mart.) pulp dietary intake improves cellular antioxidant enzymes and biomarkers of serum in healthy women. *Nutrition, 32*(6), 674-680. doi:10.1016/j.nut.2015.12.030

Bhaswant, M., Brown, L., & Mathai, M. L. (2019). Queen Garnet plum juice and raspberry cordial in mildly hypertensive obese or overweight subjects: A randomized, double-blind study. *Journal of Functional Foods, 56*, 119-126. doi:10.1016/j.jff.2019.03.011

Bloedon, T. K., Braithwaite, R. E., Carson, I. A., Klimis-Zacas, D., & Lehnhard, R. A. (2019). Impact of anthocyanin-rich whole fruit consumption on exercise-induced oxidative stress and inflammation: A systematic review and meta-analysis. *Nutrition Reviews*, *77*(9), 630-645. doi:10.1093/nutrit/nuz018

Bogdanski, P., Suliburska, J., Szulinska, M., Stepien, M., Pupek-Musialik, D., & Jablecka, A. (2012). Green tea extract reduces blood pressure, inflammatory biomarkers, and oxidative stress and improves parameters associated with insulin resistance in obese, hypertensive patients. *Nutrition research (New York, N.Y.), 32*(6), 421–427. https://doi.org/10.1016/j.nutres.2012.05.007

Bonauto, D. K., Lu, D., & Fan, Z. J. (2014). Obesity Prevalence by Occupation in Washington State, Behavioral Risk Factor Surveillance System. *Preventing Chronic Disease, 11*. doi:10.5888/pcd11.130219

Brandheim, S., Rantakeisu, U., & Starrin, B. (2013). BMI and psychological distress in 68, 000 Swedish adults: A weak association when controlling for an age-gender combination. *BMC Public Health, 13*(1). doi:10.1186/1471-2458-13-68

Browning, L. M., Hsieh, S. D., & Ashwell, M. (2010). A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0·5 could be a suitable global boundary value. *Nutrition Research Reviews*, *23*(2), 247-269. doi:10.1017/s0954422410000144

Brunzell, J. D., Davidson, M., Furberg, C. D., Goldberg, R. B., Howard, B. V., Stein, J. H., & Witztum, J. L. (2008). Lipoprotein Management in Patients With Cardiometabolic Risk: Consensus statement from the American Diabetes

Association and the American College of Cardiology Foundation. *Diabetes Care, 31*(4), 811-822. doi:10.2337/dc08-9018

Chai, S., Davis, K., Zhang, Z., Zha, L., & Kirschner, K. (2019). Effects of Tart Cherry Juice on Biomarkers of Inflammation and Oxidative Stress in Older Adults. *Nutrients, 11*(2), 228. doi:10.3390/nu11020228

Codoñer-Franch, P., Navarro-Ruiz, A., Fernández-Ferri, M., Arilla-Codoñer, Á, Ballester-Asensio, E., & Valls-Bellés, V. (2012). A matter of fat: Insulin resistance and oxidative stress. *Pediatric Diabetes, 13*(5), 392-399. doi:10.1111/j.1399-5448.2011.00847.x

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. Lawrence Erlbaum Associates.

Curtis, P. J., van der Velpen, V., Berends, L., Jennings, A., Feelisch, M., Umpleby, A. M., Evans, M., Fernandez, B. O., Meiss, M. S., Minnion, M., Potter, J., Minihane, A. M., Kay, C. D., Rimm, E. B., & Cassidy, A. (2019). Blueberries improve biomarkers of cardiometabolic function in participants with metabolic syndrome-results from a 6-month, double-blind, randomized controlled trial. *The American journal of clinical nutrition, 109*(6), 1535–1545. https://doi.org/10.1093/ajcn/nqy380

Dasgupta, S., Lokesh, S., Prasad, B. R., Saheb, S., Salman, M., Sarkar, B., & Xaviour, D. (2012). Menopause versus aging: The predictor of obesity and metabolic aberrations among menopausal women of Karnataka, South India. *Journal of Mid-life Health, 3*(1), 24. doi:10.4103/0976-7800.98814

Dohadwala, M. M., Holbrook, M., Hamburg, N. M., Shenouda, S. M., Chung, W. B., Titas, M., . . . Vita, J. A. (2011). Effects of cranberry juice consumption on vascular function in patients with coronary artery disease. *The American Journal of Clinical Nutrition, 93*(5), 934-940. doi:10.3945/ajcn.110.004242

Donato, G. B., Fuchs, S. C., Oppermann, K., Bastos, C., & Spritzer, P. M. (2006). Association between menopause status and central adiposity measured at different cutoffs of waist circumference and waist-to-hip ratio. *Menopause, 13*(2), 280-285. doi:10.1097/01.gme.0000177907.326

Dragsbæk, K., Neergaard, J. S., Laursen, J. M., Hansen, H. B., Christiansen, C., Beck-Nielsen, H., . . . Henriksen, K. (2016). Metabolic syndrome and subsequent risk of type 2 diabetes and cardiovascular disease in elderly women. *Medicine, 95*(36). doi:10.1097/md.0000000000004806

Economic Costs of Diabetes in the U.S. in 2017. (2018). *Diabetes Care, 41*(5), 917-928. doi:10.2337/dci18-0007

Emanuela, F., Grazia, M., Marco, D. R., Paola, L. M., Giorgio, F., & Marco, B. (2012). Inflammation as a Link between Obesity and Metabolic Syndrome. *Journal of Nutrition and Metabolism, 2012,* 1-7. doi:10.1155/2012/476380

Espinosa-Moncada, J., Marín-Echeverri, C., Galvis-Pérez, Y., Ciro-Gómez, G., Aristizábal, J., Blesso, C., . . . Barona-Acevedo, J. (2018). Evaluation of Agraz Consumption on Adipocytokines, Inflammation, and Oxidative Stress Markers in Women with Metabolic Syndrome. *Nutrients, 10*(11), 1639. doi:10.3390/nu10111639

Expert Panel On Detection, Evaluation, And Treatment Of High Blood Cholesterol In Adults. (2001). Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA: The Journal of the American Medical Association, 285*(19), 2486-2497. doi:10.1001/jama.285.19.2486

Feresin, R. G., Johnson, S. A., Pourafshar, S., Campbell, J. C., Jaime, S. J., Navaei, N., . . . Arjmandi, B. H. (2017). Impact of daily strawberry consumption on blood pressure and arterial stiffness in pre- and stage 1-hypertensive postmenopausal women: A randomized controlled trial. *Food & Function, 8*(11), 4139-4149. doi:10.1039/c7fo01183k

Finkelstein, E. A., Khavjou, O. A., Thompson, H., Trogdon, J. G., Pan, L., Sherry, B., & Dietz, W. (2012). Obesity and Severe Obesity Forecasts Through 2030. *American Journal of Preventive Medicine, 42*(6), 563-570. doi:10.1016/j.amepre.2011.10.026

Gangwisch, J. E., Malaspina, D., Boden-Albala, B., & Heymsfield, S. B. (2005). Inadequate Sleep as a Risk Factor for Obesity: Analyses of the NHANES I. *Sleep, 28*(10), 1289-1296. doi:10.1093/sleep/28.10.1289

García-Alonso, J., Ros, G., Vidal-Guevara, M. L., & Periago, M. J. (2006). Acute intake of phenolic-rich juice improves antioxidant status in healthy subjects. *Nutrition Research, 26*(7), 330-339. doi:10.1016/j.nutres.2006.06.004

Goss, A. M., Darnell, B. E., Brown, M. A., Oster, R. A., & Gower, B. A. (2012). Longitudinal Associations of the Endocrine Environment on Fat Partitioning in Postmenopausal Women. *Obesity, 20*(5), 939-944. doi:10.1038/oby.2011.362

Grosso, G., Stepaniak, U., Micek, A., Stefler, D., Bobak, M., & Pająk, A. (2016). Dietary polyphenols are inversely associated with metabolic syndrome in Polish adults of the HAPIEE study. *European Journal of Nutrition, 56*(4), 1409-1420. doi:10.1007/s00394-016-1187-z

Grundy, S. M., Brewer, H. B., Cleeman, J. I., Smith, S. C., & Lenfant, C. (2004). Definition of Metabolic Syndrome. *Arteriosclerosis, Thrombosis, and Vascular Biology, 24*(2). doi:10.1161/01.atv.0000111245.7575

Guo, S., Bezard, E., & Zhao, B. (2005). Protective effect of green tea polyphenols on the SH-SY5Y cells against 6-OHDA induced apoptosis through ROS–NO pathway. *Free Radical Biology and Medicine, 39*(5), 682-695. doi:10.1016/j.freeradbiomed.2005.04.022

Gurka, M. J., Vishnu, A., Santen, R. J., & Deboer, M. D. (2016). Progression of Metabolic Syndrome Severity During the Menopausal Transition. *Journal of the American Heart Association, 5*(8). doi:10.1161/jaha.116.003609

Guthrie, J. R., Dennerstein, L., Taffe, J. R., Ebeling, P. R., Randolph, J. F., Burger, H. G., & Wark, J. D. (2003). Central abdominal fat and endogenous hormones during the menopausal transition. *Fertility and sterility*, *79*(6), 1335–1340. https://doi.org/10.1016/s0015-0282(03)00361-3

Halliwell, B. (1997). Antioxidants: the basics-what they are and how to evaluate them. In: Antioxidants in disease mechanisms and therapy. *Advances in pharmacology*. Vol. 38. San Diego: Academic Press, pp. 3-20.

Harris, K. M., Majmundar, M. K., & Becker, T. (2021). *High and rising mortality rates among working-age adults*. The National Academies Press.

Higgins, J. P. T., & Thompson, S. G. (2002). Quantifying heterogeneity in a metaanalysis. *Statistics in Medicine*, *21*, 1539-1558.

Institute for Health Metrics and Evaluation. Global Burden of Disease (GBD) Compare. (2019a). University of Washington. 2021. Retrieved from https://vizhub.healthdata.org/gbd-compare/

Institute for Health Metrics and Evaluation. Tracking personal health care spending in the US. (2019b). University of Washington. 2021. Retrieved from https://vizhub.healthdata.org/dex/

Jia, X., Liu, L., Tian, Y., Wang, R., & Lu, Q. (2019). The correlation between oxidative stress level and intra-abdominal fat in obese males. *Medicine*, *98*(7). doi:10.1097/md.0000000000014469

Johnson, S. A., Figueroa, A., Navaei, N., Wong, A., Kalfon, R., Ormsbee, L. T., . . . Arjmandi, B. H. (2015). Daily Blueberry Consumption Improves Blood Pressure and Arterial Stiffness in Postmenopausal Women with Pre- and Stage 1-Hypertension: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. *Journal of the Academy of Nutrition and Dietetics*, *115*(3), 369-377. doi:10.1016/j.jand.2014.11.001 remove item

Johnson, S. A., Feresin, R. G., Navaei, N., Figueroa, A., Elam, M. L., Akhavan, N. S., . . . Arjmandi, B. H. (2017). Effects of daily blueberry consumption on circulating biomarkers of oxidative stress, inflammation, and antioxidant defense in postmenopausal women with pre- and stage 1-hypertension: A randomized controlled trial. *Food & Function, 8*(1), 372-380. doi:10.1039/c6fo01216g

Jung, U. J., Kim, H. J., Lee, J. S., Lee, M. K., Kim, H. O., Park, E. J., Kim, H. K., Jeong, T. S., & Choi, M. S. (2003). Naringin supplementation lowers plasma lipids and enhances erythrocyte antioxidant enzyme activities in hypercholesterolemic subjects. *Clinical nutrition (Edinburgh, Scotland), 22*(6), 561–568. https://doi.org/10.1016/s0261-5614(03)00059-1

Jung, U., & Choi, M. (2014). Obesity and Its Metabolic Complications: The Role of Adipokines and the Relationship between Obesity, Inflammation, Insulin Resistance, Dyslipidemia and Nonalcoholic Fatty Liver Disease. *International Journal of Molecular Sciences, 15*(4), 6184-6223. doi:10.3390/ijms15046184

Kahn, R., Buse, J., Ferrannini, E., & Stern, M. (2005). The Metabolic Syndrome: Time for a Critical Appraisal: Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care, 28*(9), 2289-2304. doi:10.2337/diacare.28.9.2289

Kanellos, P. T., Kaliora, A. C., Protogerou, A. D., Tentolouris, N., Perrea, D. N., & Karathanos, V. T. (2017). The effect of raisins on biomarkers of endothelial function and oxidant damage; an open-label and randomized controlled

intervention. *Food Research International, 102*, 674-680. doi:10.1016/j.foodres.2017.09.061

Kershaw, E. E., & Flier, J. S. (2004). Adipose Tissue as an Endocrine Organ. *The Journal of Clinical Endocrinology & Metabolism, 89*(6), 2548-2556. doi:10.1210/jc.2004-0395

Khoubnasabjafari, M., Ansarin, K., & Jouyban, A. (2015). Reliability of malondialdehyde as a biomarker of oxidative stress in psychological disorders. *BioImpacts : BI, 5*(3), 123–127. https://doi.org/10.15171/bi.2015.20

Kim, H. M., Park, J., Ryu, S. Y., & Kim, J. (2007). The Effect of Menopause on the Metabolic Syndrome Among Korean Women: The Korean National Health and Nutrition Examination Survey, 2001. *Diabetes Care, 30*(3), 701-706. doi:10.2337/dc06-1400

Kolehmainen, M., Mykkänen, O., Kirjavainen, P. V., Leppänen, T., Moilanen, E., Adriaens, M., . . . Törrönen, R. (2012). Bilberries reduce low-grade inflammation in individuals with features of metabolic syndrome. *Molecular Nutrition & Food Research, 56*(10), 1501-1510. doi:10.1002/mnfr.201200195

Lee, Y., Thacker, R., Hall, B., Kong, R., & Granneman, J. G. (2014). Exploring the activated adipogenic niche: Interactions of macrophages and adipocyte progenitors. *Cell Cycle, 13*(2), 184-190. doi:10.4161/cc.27647

Litvinov, D., Mahini, H., & Garelnabi, M. (2012). Antioxidant and anti-inflammatory role of paraoxonase 1: implication in arteriosclerosis diseases. *North American*

journal of medical sciences, 4(11), 523–532. https://doi.org/10.4103/1947-2714.103310

Lizcano, F., & Guzmán, G. (2014). Estrogen Deficiency and the Origin of Obesity during Menopause. *BioMed Research International, 2014*, 1-11. doi:10.1155/2014/757461

Loo, B., Erlund, I., Koli, R., Puukka, P., Hellström, J., Wähälä, K., . . . Jula, A. (2016). Consumption of chokeberry (Aronia mitschurinii) products modestly lowered blood pressure and reduced low-grade inflammation in patients with mildly elevated blood pressure. *Nutrition Research, 36*(11), 1222-1230. doi:10.1016/j.nutres.2016.09.005 remove item

Lynn, A., Mathew, S., Moore, C. T., Russell, J., Robinson, E., Soumpasi, V., & Barker, M. E. (2014). Effect of a Tart Cherry Juice Supplement on Arterial Stiffness and Inflammation in Healthy Adults: A Randomised Controlled Trial. *Plant Foods for Human Nutrition, 69*(2), 122-127. doi:10.1007/s11130-014-0409-x

Mendonça, R., Carvalho, N., Martin-Moreno, J., Pimenta, A., Lopes, A., Gea, A., . . . Bes-Rastrollo, M. (2019). Total polyphenol intake, polyphenol subtypes and incidence of cardiovascular disease: The SUN cohort study. *Nutrition, Metabolism and Cardiovascular Diseases, 29*(1), 69-78. doi:10.1016/j.numecd.2018.09.012

Moazen, S., Amani, R., Rad, A. H., Shahbazian, H., Ahmadi, K., & Jalali, M. T. (2013). Effects of Freeze-Dried Strawberry Supplementation on Metabolic Biomarkers of Atherosclerosis in Subjects with Type 2 Diabetes: A Randomized Double-Blind

Controlled Trial. *Annals of Nutrition and Metabolism, 63*(3), 256-264. doi:10.1159/000356053

Moncada S. (2006). Adventures in vascular biology: a tale of two mediators. Philosophical transactions of the Royal Society of London. *Series B, Biological sciences, 361*(1469), 735–759. https://doi.org/10.1098/rstb.2005.1775

Nakagawa, T., & Yokozawa, T. (2002). Direct scavenging of nitric oxide and superoxide by green tea. *Food and Chemical Toxicology, 40*(12), 1745-1750. doi:10.1016/s0278-6915(02)00169-2

National Center for Health Statistics. Health, United States, 2019: Table 006. Hyattsville, MD. 2021. Available from: https://www.cdc.gov/nchs/hus/contents2019.htm

Paneni, F., Costantino, S., & Cosentino, F. (2015). Role of oxidative stress in endothelial insulin resistance. *World journal of diabetes, 6*(2), 326–332. https://doi.org/10.4239/wjd.v6.i2.326

Perry, A., Wang, X., Goldberg, R., Ross, R., & Jackson, L. (2013). Androgenic sex steroids contribute to metabolic risk beyond intra-abdominal fat in overweight/obese black and white women. *Obesity, 21*(8), 1618-1624. doi:10.1002/oby.20204

Pham-Huy, L. A., He, H., & Pham-Huy, C. (2008). Free radicals, antioxidants in disease and health. *International journal of biomedical science : IJBS, 4*(2), 89–96.

Rahbar, A. R., Mahmoudabadi, M. M., & Islam, M. S. (2015). Comparative effects of red and white grapes on oxidative markers and lipidemic parameters in adult

hypercholesterolemic humans. *Food & Function, 6*(6), 1992-1998. doi:10.1039/c5fo00100e

Razmjou, S., Abdulnour, J., Bastard, J., Fellahi, S., Doucet, É, Brochu, M., . . . Prud'Homme, D. (2018). Body composition, cardiometabolic risk factors, physical activity, and inflammatory markers in premenopausal women after a 10-year follow-up: A MONET study. *Menopause, 25*(1), 89-97. doi:10.1097/gme.0000000000000951

Ridker, P. M., Rifai, N., Rose, L., Buring, J. E., & Cook, N. R. (2002). Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. *The New England journal of medicine, 347*(20), 1557–1565. https://doi.org/10.1056/NEJMoa021993

Sapkota, A. S., Sapkota, A., Acharya, K., Raut, M., & Jha, B. (2015). Study of metabolic syndrome in postmenopausal women. *Annals of Clinical Chemistry and Laboratory Medicine, 1*(1), 6-11. doi:10.3126/acclm.v1i1.12307

Scalbert, A., & Williamson, G. (2000). Dietary Intake and Bioavailability of Polyphenols. *The Journal of Nutrition, 130*(8). doi:10.1093/jn/130.8.2073s

Sohrab, G., Ebrahimof, S., Sotoudeh, G., Neyestani, T. R., Angoorani, P., Hedayati, M., & Siasi, F. (2016). Effects of pomegranate juice consumption on oxidative stress in patients with type 2 diabetes: A single-blind, randomized clinical trial. *International Journal of Food Sciences and Nutrition, 68*(2), 249-255. doi:10.1080/09637486.2016.1229760

Sproston, N. R., & Ashworth, J. J. (2018). Role of C-Reactive Protein at Sites of Inflammation and Infection. *Frontiers in immunology, 9*, 754. https://doi.org/10.3389/fimmu.2018.00754

Stefanska, A., Bergmann, K., & Sypniewska, G. (2015). Metabolic Syndrome and Menopause. *Advances in Clinical Chemistry*, 1-75. doi:10.1016/bs.acc.2015.07.001

Stote, K. S., Sweeney, M. I., Kean, T., Baer, D. J., Novotny, J. A., Shakerley, N. L., . . . Gottschall-Pass, K. T. (2017). The effects of 100% wild blueberry (Vaccinium angustifolium) juice consumption on cardiometablic biomarkers: A randomized, placebo-controlled, crossover trial in adults with increased risk for type 2 diabetes. *BMC Nutrition, 3*(1). doi:10.1186/s40795-017-0164-0

Strack D, Wray V. The Anthocyanins: The Flavonoids: Advances in Research since 1986. London, UK: Chapman and Hall; 1993.

Trapp, C., & Levin, S. (2012). Preparing to Prescribe Plant-Based Diets for Diabetes Prevention and Treatment. *Diabetes Spectrum, 25*(1), 38-44. doi:10.2337/diaspect.25.1.38

Tsikas D. (2017). Assessment of lipid peroxidation by measuring malondialdehyde (MDA) and relatives in biological samples: Analytical and biological challenges. *Analytical biochemistry, 524*, 13–30. https://doi.org/10.1016/j.ab.2016.10.021

Tuso, P. J., Ismail, M. H., Ha, B. P., & Bartolotto, C. (2013). Nutritional update for physicians: plant-based diets. *The Permanente journal, 17*(2), 61–66. https://doi.org/10.7812/TPP/12-085

Weinberg, M. E., Manson, J. E., Buring, J. E., Cook, N. R., Seely, E. W., Ridker, P. M., & Rexrode, K. M. (2006). Low sex hormone–binding globulin is associated with the metabolic syndrome in postmenopausal women. *Metabolism, 55*(11), 1473-1480. doi:10.1016/j.metabol.2006.06.017

Weisberg, S. P., Mccann, D., Desai, M., Rosenbaum, M., Leibel, R. L., & Ferrante, A. W. (2003). Obesity is associated with macrophage accumulation in adipose tissue. *Journal of Clinical Investigation, 112*(12), 1796-1808. doi:10.1172/jci200319246

WHO Consultation on Obesity (1999: Geneva, Switzerland) & World Health Organization. (2000). Obesity : preventing and managing the global epidemic : report of a WHO consultation. World Health Organization. https://apps.who.int/iris/handle/10665/42330

Yan, Z., Zhong, Y., Duan, Y., Chen, Q., & Li, F. (2020). Antioxidant mechanism of tea polyphenols and its impact on health benefits. *Animal Nutrition, 6*(2), 115-123.

Yiannakopoulou, E. C. (2013). Targeting oxidative stress response by green tea polyphenols: Clinical implications. *Free Radical Research, 47*(9), 667-671. doi:10.3109/10715762.2013.819975 doi:10.1016/j.aninu.2020.01.001

Zhang, Y., Proenca, R., Maffei, M., Barone, M., Leopold, L., & Friedman, J. M. (1994). Positional cloning of the mouse obese gene and its human homologue. *Nature, 372*(6505), 425-432. doi:10.1038/372425a0

Zheng, X. X., Xu, Y. L., Li, S. H., Liu, X. X., Hui, R., & Huang, X. H. (2011). Green tea intake lowers fasting serum total and LDL cholesterol in adults: a meta-analysis

of 14 randomized controlled trials. *The American journal of clinical nutrition, 94*(2), 601–610. https://doi.org/10.3945/ajcn.110.010926

Zhu, Y., Ling, W., Guo, H., Song, F., Ye, Q., Zou, T., Li, D., Zhang, Y., Li, G., Xiao, Y., Liu, F., Li, Z., Shi, Z., & Yang, Y. (2013). Anti-inflammatory effect of purified dietary anthocyanin in adults with hypercholesterolemia: a randomized controlled trial. *Nutrition, metabolism, and cardiovascular diseases : NMCD, 23*(9), 843–849. https://doi.org/10.1016/j.numecd.2012.06.005

Ziaei, S., & Mohseni, H. (2013). Correlation between Hormonal Statuses and Metabolic Syndrome in Postmenopausal Women. *Journal of family & reproductive health, 7*(2), 63–66.

Appendix

Table 1

Simplified Study Coding Sheet

Study	Food	Processing Method	Dose	Total Anthocya	Delivery Schedule	Design	Duration	Treatment (N)	Control (N)	Sex/Age	Health Status	Weight Category	Menopause Status
Arevstrom et al.,	Bilberry	Freeze-dried	40 g	2250	DM	Exp	8 wk	25	25	MF/>55	C	H, OW	Post
Asgary et al., 2014	Pomegranate	Juice Fresh	150 ml	8.7	DS	Exp	2 wk	11	10	MF/24-55	C	H, OW	Mix
Aviram et al., 2004	pomegranate	Juice Fresh	500 ml	19.2	DS	Exp	36 mo	10	10	MF/>55	C	H, OW	Post
Barbosa et al.,	Acai	Flash Frozen	200 g	262	DS	Exp	4 wk	35	35	F/24-55	NC	H	Mix
Bardagjy et al.,	Grape, red	Freeze-dried	60 g	27.5	DS	X-O	4 wk	20	20	MF/24-55	NC	Ob	Mix
Basu et al., 014	Strawberry	Freeze-dried	25 g	78	DM	Exp	12 wk	15	15	MF/24-55	C	Ob	Mix
Basu et al., 2009	Strawberry	Freeze-dried	50 g	154	DM	Q-Exp	4 wk	16	16	F/24-55	C	Ob	Mix

Study	Dohadwala et al.,	Desai et al., 2018	Davidson et al.,	Chai et al., 2019	Burton-Freeman	Boldagi et al., 2019	Bialasiewicz et al.,	Bhaswant et al.,	Basu et al., 2010
Food	Cranberry	Cherry, tart	Pomegranate	Cherry, tart	Strawberry	Pomegranate	Cherry, tart	Plum	Strawberry
Processing Method	Juice Fresh	Juice Concentrat	Juice Fresh	Juice Concentrat	Freeze-dried	Juice Fresh	Fresh Whole	Juice Fresh	Freeze-dried
Dose	480 ml	60 ml	240 ml	68 ml	10 g	100 ml	500 g	250 ml	50 g
Total Anthocya	94	540	24	612	31	10	346.5	102	154
Delivery Schedule	DS	DM	DM	DM	DS	DS	DS	DS	DM
Design	X-O	X-O	Exp	Exp	X-O	X-O	Exp	Exp	Exp
Duration	4 wk	20 da	18 mo	12 wk	6 wk	8 wk	30 da	12 wk	8 wk
Treatment (N)	22	11	146	17	24	41	34	15	15
Control (N)	22	11	143	17	24	41	34	14	12
Sex/Age	MF/>55	MF/ 24-55	MF/>55	MF/>55	MF/24-55	MF/24-55	MF/24-55	MF/24-55	MF/24-55
Health Status	C	NC	C	NC	C	C	NC	C	C
Weight Category	OW, Ob	H	OW, Ob	OW	OW, Ob	H, OW	H	OW, Ob	Ob
Menopause Status	Post	Mix	Post	Post	Mix	Mix	Mix	Mix	Mix

Study	Kanellos et al.,	Johnson et al.,	Johnson et al.,	Jenkins et al., 2008	Habanova et al.,	Guo et al., 2008	Garcia-Alonso et	Feresin et al., 2017	Espinosa-Moncada
Food	Grape, red	Blueberry	Blueberry	Strawberry	Bilberry	Pomegranate	Blend (grape+cher	Strawberry	Agraz
Processing Method	Dried	Freeze-dried	Freeze-dried	Fresh Whole	Flash Frozen	Juice Fresh	Juice Concentrate	Freeze-dried	Freeze-dried
Dose	36 g	22 g	22 g	454 g	150 g	250 ml	400 ml	25 g	200 ml
Total Anthocya	16.5	469	469	150	456	25	286	102	932
Delivery Schedule	DS	DM	DM	DS	DS	DS	SS	DM	DS
Design	Exp	Exp	Exp	X-O	X-O	Exp	Q-Exp	Par	X-O
Duration	24 wk	8 wk	8 wk	4 wk	6 wk	4 wk	Acute	8 wk	4 wk
Treatment (N)	26	20	20	28	25	13	12	20,20	37
Control (N)	22	20	20	28	25	13	12	20	37
Sex/Age	MF/>55	F/24-55	F/24-55	MF/>55	F/24-55	MF/>55	MF/24-55	F/>55	F/24-55
Health Status	C	C	C	C	NC	NC	NC	C	C
Weight Category	OW, Ob	NA	OW, Ob	OW	H, OW	H, OW	H	Ob	OW, Ob
Menopause Status	Post	Post	Post	Post	Mix	Post	Mix	Post	Mix

Study	Lynn et al., 2012	Loo et al., 2016	Kolehmainen et al.,	Kojadinovic et al.,	Kent et al., 2017	Kelley et al., 2013	Kardum et al.,	Kardum et al.,	Kanellos et al.,
Food	Pomegranate	Chokeberry	Bilberry	Pomegranate	Cherry, Sweet	Cherry, Sweet	Chokeberry	Chokeberry	Grape, red
Processing Method	Juice Fresh	Oven-Dried	Fresh Puree+Fre	Juice Fresh	Juice Fresh	Fresh Whole	Juice Fresh	Juice Fresh	Dried
Dose	330 ml	3g + 300 ml	200g + 40g	300 ml	200 ml	280 g	200 ml	100 ml	90 g
Total Anthocya	33	1024	1380.8	6.3	138	84	298	25	41
Delivery Schedule	DS	DM	DS	DS	DS	DS	DS	DS	DS
Design	Exp	X-O	Exp	Exp	Exp	Q-Exp	Q-Exp	Q-Exp	Exp
Duration	4 wk	8 wk	8 wk	6 wk	12 wk	4 wk	4 wk	12 wk	4 wk
Treatment (N)	22	37	13	12	24	18	23	29	22
Control (N)	24	37	11	11	25	18	23	29	14
Sex/Age	MF/24-55	MF/>55	MF/24-55	F/24-55	MF/>55	MF/24-55	MF/24-55	F/24-55	MF/24-55
Health Status	NC	C	C	C	C	NC	C	NC	NC
Weight Category	H, OW	H, OW	OW, Ob	H, OW	H, OW	OW	NA	H, OW	H
Menopause Status	Mix	Post	Mix	Mix	Post	Mix	Mix	Mix	Mix

Study	Sohrab et al., 2017	Sohrab et al., 2015	Small et al., 2014	Shishehbor et al.,	Rahbar et al., 2015	Pokimica et al.,	Moazzen et al.,	Moazzen et al.,	Lynn et al., 2014
Food	Pomegranate	Pomegranate	Grape, red	Pomegranate	Grape, red, white	Chokeberry	Pomegranate	Strawberry	Cherry, tart
Processing Method	Juice Fresh	Juice Fresh	Freeze-dried	Juice Concentrat	Fresh Whole	Juice Fresh	Juice Fresh	Freeze-dried	Juice Concentrat
Dose	200 ml	250 ml	47 g	50 ml	500 g	100 ml	500 ml	50 g	30 ml
Total Anthocya	20	25	32.9	2.05	42	294	50	154	273.5
Delivery Schedule	DS	DS	DS	DS	DM	SS	DS	DM	DS
Design	Exp	Exp	Exp	Q-Exp	Par	Par	X-O	Exp	Exp
Duration	6 wk	12 wk	16 wk	4 wk	8 wk	4 wk	1 wk	6 wk	6 wk
Treatment (N)	30	22	35	31	22,24	27,27	30	19	22
Control (N)	30	22	34	31	23	26	30	17	17
Sex/Age	MF/>55	MF/>55	MF/>55	MF/24-55	MF/24-55	F/24-55	MF/24-55	MF/24-55	MF/24-55
Health Status	C	C	NC	C	C	C	C	C	NC
Weight Category	OW	OW, Ob	OW, Ob	OW	OW, Ob	H, OW	NA	OW	H, OW
Menopause Status	Post	Post	Post	Mix	Mix	Mix	Mix	Mix	Mix

Study	Food	Processing Method	Dose	Total Anthocya	Delivery Schedule	Design	Duration	Treatment (N)	Control (N)	Sex/Age	Health Status	Weight Category	Menopause Status
Stote et al., 2017	Wild Blueberry	Juice Fresh	240 ml	314	DS	X-O	1 wk	19	19	F/24-55	C	OW, Ob	Post
Tulipani et al.,	Strawberry	Fresh Whole	500 g	150	DM	Q-Exp	2 wk	12	12	MF/24-55	NC	H	Pre
Zemenu et al., 2013	Grape, red	Freeze-dried	46 g	32.2	DS	Par	12 wk	11	14	F/24-55	NC	OW, Ob	Post
Zunino et al., 2014	Grape, red	Freeze-dried	92 g	42	DM	X-O	3 wk	24	24	MF/24-55	NC	Ob	Pre

Note: Delivery schedule: DS-daily single; DM-daily multiple; SS-single serving only. Design: Exp-experimental; X-O-crossover; Par-parallel; Q-Exp-quasi-experimental. Sex/Age: MF-male, female. Health status: NC-no (existing health) conditions; C-(existing) condition. Weight category: H-healthy; OW-overweight; Ob-obese. Menopause status: Pre-pre-menopause; Post-post-menopause; Mix-pre and post-menopause.