Project on

A review on Potential therapeutic effect of antioxidant food components based on molecular mechanism in the treatment of Cardiovascular diseases

A dissertation submitted to the Department of Pharmacy, Daffodil International University, slightly fulfils the needs for the Bachelor of Pharmacy degree (B. Pharm).

Submitted To

The Department of Pharmacy

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In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

Submitted By

Student ID: 191-29-1476

Batch: 21

Department of Pharmacy

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APPROVAL

This project **'A review on Potential therapeutic effect of antioxidant food components based on molecular mechanism in the treatment of Cardiovascular diseases'** submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

Board of Examiners

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Internal Examiner 1

Internal Examiner 2

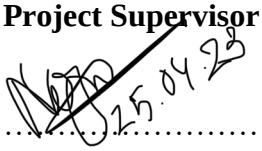
External Examine

CERTIFICATION

Dissertation Acceptance Form Daffodil International University, Department of Pharmacy.

This is to certify that the results of investigation of this project works are original & have not been submitted before in this University. This entire project work has been accepted satisfactory requirements for Bachelor of Pharmacy.

Project Supervisor



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Declaration

I, with this, declare that I do this project under the supervision of Nazneen Ahmeda Sultana, Assistant Professor, Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, and reasonably meet the requirements of a Bachelor of Pharmacy (B. Pharm) degree. I declare that this project is entirely my creation. I further certify that the implementations in this project are unique and have never been submitted to any degree program at this university.

Submitted By

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Acknowledgement

First and foremost, I would like to convey my heartfelt gratitude to the Almighty God for giving me the chance to study this subject, the capability to complete my project work, and finally the ability to write up the project work & results in order to fulfill the requirements for the Bachelor of Pharmacy degree. I would like to express my deepest appreciation and respect to my honorable supervisor Nazneen Ahmeda Sultana (Assistant Professor) Department of Pharmacy, Daffodil International University.

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Abstract

Cardiovascular diseases (CVDs) have recently come to the forefront due to their alarmingly rising incidence and mortality rate. Epidemiological studies have revealed that those who eat a diet high in whole grains, fruits, vegetables, and nuts have a decreased chance of developing cardiovascular disease. Consuming a broad array of antioxidant natural products and the bioactive components of these substances greatly enhanced the cardiovascular health of the research participants. Puerarin may include high levels of antioxidants such polyphenols, polysaccharides, anthocyanins, epigallocatechin gallate, quercetin, rutin, and others. These results may arise from changes in blood pressure, lipid profiles, oxidative stress, inflammation, and maybe even the makeup of gut flora. Numerous studies have indicated that eating antioxidant-rich foods including soursop, beetroot, garlic, almonds, and green tea improves cardiovascular health. With a focus on clarifying underlying processes and reporting clinical trials, we collated data from epidemiological, experimental, and clinical studies evaluating the effect of diverse antioxidant natural products and their bioactive components on cardiovascular disorders.

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CHAPTER -01

INTRODUCTION

1. Introduction

According to the World Health Organisation (WHO), 25 percent of all deaths worldwide are caused by cardiovascular disease [1]. The phrase "cardiovascular disease" (CVD) refers to a group of conditions that includes heart failure, stroke, excessive blood pressure, and coronary heart disease (CHD). The occurrence of cardiovascular disease has been linked to a wide range of factors [2, 3]. This category of diseases includes oxidative stress, intestinal dysbiosis, dyslipidemia, hypertension, and atherosclerosis. Synthetic medications used to treat cardiovascular diseases are associated with a wide variety of undesired side effects [5, 6], including hyperkalemia, arrhythmias, and gastrointestinal issues. These are only few of the many possible negative reactions. However, there is mounting evidence that natural antioxidants may be utilised safely and effectively in the management of cardiovascular diseases [7–11]. Numerous illnesses and ailments, such as obesity, cancer, inflammation, liver damage, and cardiovascular disease, have been linked to a reduction in natural product consumption. In addition to all of these advantages, they are also a good source of essential nutrients such fibre, flavonoids, vitamins, and minerals [12-15]. Fruits, vegetables, teas, cereals, and nuts are all good sources of antioxidants, and eating them regularly has been shown in epidemiological studies to significantly lower the risk of cardiovascular disease [16,17]. Many research [18–20] have shown the efficacy of certain antioxidant natural products and their active components in the treatment and prevention of CVDs. Several naturally occurring antioxidant molecules have been found to be useful in the treatment and prevention of cardiovascular disorders in human clinical investigations [21]. This review aims to synthesise the results of epidemiological, experimental, and clinical investigations conducted over the last decade on the impact of a specific class of naturally occurring antioxidants and the bioactive components of those antioxidants on cardiovascular diseases. The study's major emphasis was on the clinical application of these medicines.

CHAPTER- 02

GOAL OF MY STUDY

2.1 Goal of My Study

The goal of the study is:

- To know about the antioxidant food component products.
- To know about source of natural antioxidant.
- To learn which type of plants contains antioxidant activity.
- To find out natural antioxidant mechanism for cardiovascular disease.
- To ascertain the diagnosis and natural treatment options of cardiovascular disease.
- To understand more about cardiovascular risk factor.

CHAPTER- 03

METHODOLGY

3.1 Methodology

3.2. Introduction

The examination is preceded with a literature study. For this study, 50 or so publications are reviewed.

3.3. Research Design

This exploration was planned through Google scholar, PubMed and many other websites to find literature. For referencing mendeley software was used.

3.4. Method of Data Analysis

After gathering a variety of data, each piece was examined for accuracy and internal coherence to rule out any missing or inconsistent pieces, and those were then deleted. Information research was carried out using Microsoft's dominant updated version. All data was gathered between 2012 and 2022.

3.5. Ethical Considerations

The members of the investigation were spoken to and given the go-ahead verbally for the information gathering process. The respondents' identities were kept secret, and participants in the study were informed that they may drop out at any point during the information gathering process. The study was sponsored by the Department of Pharmacy.

CHAPTER- 04

Epidemiology

4.1 Epidemiology

Table 1: Epidemiological studies

Plants	Study type	Subjects	Results	Reference
Fruit	A cross-sectional analysis	1,590 adults	In the 50-59 age group, less fruit consumption was linked to higher blood pressure (PR: 1.62; 95% CI, 1.09-2.41).	[22]
Fruit	Cohort analysis	70,047 Chinese adults with CVD or hypertension	correlated negatively with death from cardiovascular disease (HR = 0.79; 95% CI = 0.73-0.86).	[23]
Vegetable	A Cross-sectional analysis	18,757 adolescents	Risk of hypertension was reduced (OR, 0.74; 95% CI, 0.58-0.94) among those who ate at least three servings of vegetables each day.	[24]
Allium vegetable	Cohort analysis	Adult men and women	Risk of CVD events reduced by 64% (HR: 0.36; 95% CI: 0.18-0.71)	[25]
Nut	3 significant cohort analysis	34,103 men 77,815 women 80,737 women	linked negatively to CHD (RR 0.94, 95% CI 0.89-0.99), stroke (RR 0.89, 95% CI 0.83-0.95), and CVD (RR 0.92, 95% CI 0.86-0.98).	[26]
Fruit, vegetable	A Cross-sectional analysis	1,596 adolescents and young people in Tanzania and Uganda	Reduces hypertension risk (OR = 0.7; 95% CI = 0.50-0.98).	[27]
Fruit, vegetable	A Cross-sectional analysis	229 patients with primary hypertension	The reduction of blood pressure, heart rate, and body mass index	[28]

Many epidemiological studies have shown that plant-based diets can prevent and even treat cardiovascular disease. Researchers in China found that among 18,757 young adults, the risk of developing hypertension was reduced among those who had three or more servings of vegetables daily [24]. Fist sizes in the male gender tend to be around the same as a single serve. This investigation was carried out by Chinese researchers. Several cohort studies have found that those who eat a plant-based diet had a lower chance of developing cardiovascular disease. There was a

significant difference in the systolic blood pressure (SBP) and blood glucose levels of 521,891 Chinese adults aged 30-79 who ate fresh fruit on a regular basis and those who did not. This was evident when comparing consistent usage to less frequent usage or no usage at all, as predicted. Between 0.75 and 0.79 was the risk ratio for an ischemic stroke, whereas it was between 0.52 and 0.74 for a hemorrhagic stroke, 0.66 and 0.75 for an incident major coronary event, and between 0.50 and 0.67 for mortality due to cardiovascular disease. [26]. Eating allium plants like garlic and onion was linked to a 64% decrease in cardiovascular disease outcomes (HR= 0.36; 95% CI: 0.18-0.71) [27] in a different experiment with 3,052 individuals. In a study of young individuals in the Mediterranean, the Human Relative Hazard (95% Confidence Interval) for those in the highest quintiles of fruit and whole grain eating was 0.51 [0.27-0.95], and for those in the highest quintiles of whole grain consumption, it was 0.43 [0.20-0.93]. According to a second prospective study involving 2,295 Iranians, individuals who consumed the most dietary fibre from fruits, vegetables, cereals, legumes, nuts, and other sources had a decreased risk of cardiovascular disease than those who consumed the least. The hazard ratios (HR) for cardiovascular disease were 0.90 (0.44-1.86), 0.31 (0.15-0.52), 0.49 (0.24-1.02), and 0.44 (0.22-0.89), in that order. However, a cohort study found a significantly decreased risk of cardiovascular disease associated with nut consumption [28]. It is unclear if the advantage of nuts in lowering the risk of cardiovascular disease (CVD) is due to the nuts themselves or the bioactive elements they contain, such as dietary fibre. Emerging data from epidemiological studies suggests that these products' bioactive components and some naturally occurring antioxidant compounds may work as a defence against cardiovascular disease (CVD). However, there is no guarantee of the results. Fresh vegetables, cereals, legumes, nuts, and other plant-based diets have all been linked to a reduced risk of cardiovascular diseases (CVDs). Many different plants may offer defence against cardiovascular diseases, according to growing body of scientific research. Because there is an inverse correlation between the risk of cardiovascular disease and consumption of such foods, avoiding plant-based meals can reduce a person's likelihood of getting the condition.

CHAPTER -05

Literature review

5.1 Dietary fruits and vegetables and cardiovascular diseases risk. Critical reviews in food science and nutrition. [29].

The majority of the topics discussed in the article relate to bioactive compounds, food, heart disease, diabetes, obesity, and diseases including hypertension and hypertension. We examine the data supporting the idea that a diet rich in fruits and vegetables reduces the risk of cardiovascular disease in this article. Eating a diet high in fruits and vegetables may help lower the prevalence of cardiovascular disease (CVD), according to early data from observational studies. Ongoing discussion surrounds the recommended amount of meals, which may not be five, as well as their possible impacts. It is impossible to show via the use of randomised controlled trials that a diet rich in fruits and vegetables protects cardiovascular disease. Due to their high energy content, low glycemic load, and other bioactive nutritional benefits, fruits and vegetables can be used as a preventative approach. In order to reduce the risk of CVD, dietary patterns and consuming whole meals may be more important to focus on than specific nutrients, according to a recent study, considering the complicated interplay between various nutrients and possibly genetic risk factors. A fuller knowledge of the link between eating fruits and vegetables and cardiovascular risk would be very beneficial for health professionals in order to properly focus clinical practises and public health [29].

5.2 Food antioxidants and their anti-inflammatory properties: a potential role in cardiovascular diseases and cancer prevention. Diseases. [30].

This study looks at the connections between stress, inflammation, transcription factors, the microbiome, vitamins, pro-oxidants, flavonoids, and carotenoids. Numerous studies from the past indicate that adopting a Mediterranean-style diet has a significant detrimental effect on the incidence of cardiovascular illnesses (CVDs). According to a study that examined how diet impacted the oxidation of lipoproteins, people who followed the Mediterranean diet and used virgin olive oil experienced much lower levels of oxidative stress than those who ate low-fat meals. There has been much research into the mechanisms behind the interventional stimulation of apoptosis, the effects of these processes on cancer and cardiovascular disease, the inhibition of proliferation, inflammation, invasion, and metastasis, as well as the activation of apoptosis. Fruits, vegetables, tea, and wine all contain flavonoid antioxidants, which are compounds having 2- or 3-phenylchroman structures. It has been proven that these compounds aid in the prevention of heart

disease and cancer. Flavonoids like luteolin, quercetin, kaempferol, myricetin, and apigenin are among them. Flavonoids can defend DNA against hydroxyl radical damage through the crucial chelation step. In the hopes that they will one day be a successful substitute for conventional pharmaceutical therapies, the primary and secondary human metabolomes have been explored [30].

5.3 Antioxidant food components for the prevention and treatment of cardiovascular diseases: effects, mechanisms, and clinical studies. Oxidative medicine and cellular longevity. [31].

The results of this study indicate that increasing the intake of fruits, vegetables, nuts, and cereals may reduce the prevalence of cardiovascular diseases (CVDs), with the antioxidants included in these foods serving as the main protective element. The objective of this article is to summarise the results of epidemiological, experimental, and clinical research on cardiovascular diseases (CVDs) conducted over the past five years looking at the effects of various antioxidant natural products and their bioactive components. On clinical trials and how they work, there will be a lot of emphasis. This study also shows that a variety of naturally occurring foods, like fruits, vegetables, and nuts, have antioxidant properties that can lower blood pressure, inflammation, RAS, boost nitric oxide levels, improve lipid profiles, and lower the risk of cardiovascular disease. When 45 healthy students consume 400 grammes of guava daily, blood pressure, triglycerides, and LDL cholesterol levels decrease. Some individuals, including men, women, and the elderly, are advised to consume meals that contain vegetables, tomato extract, and carrot juice in order to reduce their chance of developing cardiovascular disease [31].

CHAPTER -06
Result & Discussion

6. Results and Discussion

6.1. The effects of antioxidant natural products on CVDs from experimental studies

6.1.1. Result

Table 2: The effects of antioxidant natural products on CVDs from experimental studies.

Plants	Components	Study type	Effects and mechanisms	Reference
Winged bean seed	Peptide	*In vitro* *In vivo*	Blocking ACE Enzyme Activity reduction in blood pressure	[32]
Solanum macrocarpon	Polyphenols	*In vitro* *In vivo*	Reducing the production of ACE and renin Reduced blood pressure and heart rate	[33]
Pigeon pea	Protein	*In vitro* *In vivo*	blocking ACE and renin enzymes and mopping up free radicals reduction in blood pressure	[34]
Tea	Polyphenols	*In vivo*	Reducing total and low-density lipoprotein cholesterol and plaque area/lumen area	[35]
White mulberry fruit	Polysaccharides	*In vitro* *In vivo*	Relaxation of the endothelium and release of	[36]

			nitric oxide in the arteries of the rat mesenteric gland. Decreases in systolic and diastolic blood	
Rice bran	Protein	*In vivo*	Reducing Blood Pressure (ACE↓, NO, and eNOS↑)	[37]
Lycium ruthenicum Murray	Anthocyanins	*In vivo*	Enhanced resistance to oxidative stress and inflammation	[38]

6.1.2 Discussion

By simulating the enzyme as a peptide and the plant as a bean seed, this table demonstrates that lowering ACE enzyme activity lowers blood pressure in both in vitro and in vivo tests. On bean seeds, in vitro research was done. Through research carried out under both vitro and in vivo circumstances, it has been demonstrated that the polyphenolic component of Solanum macrocarpon can lower blood pressure and heart rate. The reduction of total cholesterol, low-density lipoprotein cholesterol, and plaque area by tea plant extracts has been demonstrated in studies on living animals. Increased resilience to oxidative and inflammatory stress is seen in plants from the Lyceum ruthenium Murray genus. According to this study, eating a few certain plant species can lower your chance of developing cardiovascular problems.

6.2. The relevant mechanisms of some antioxidant natural products and their bioactive compounds on CVDs

6.2.1. Result

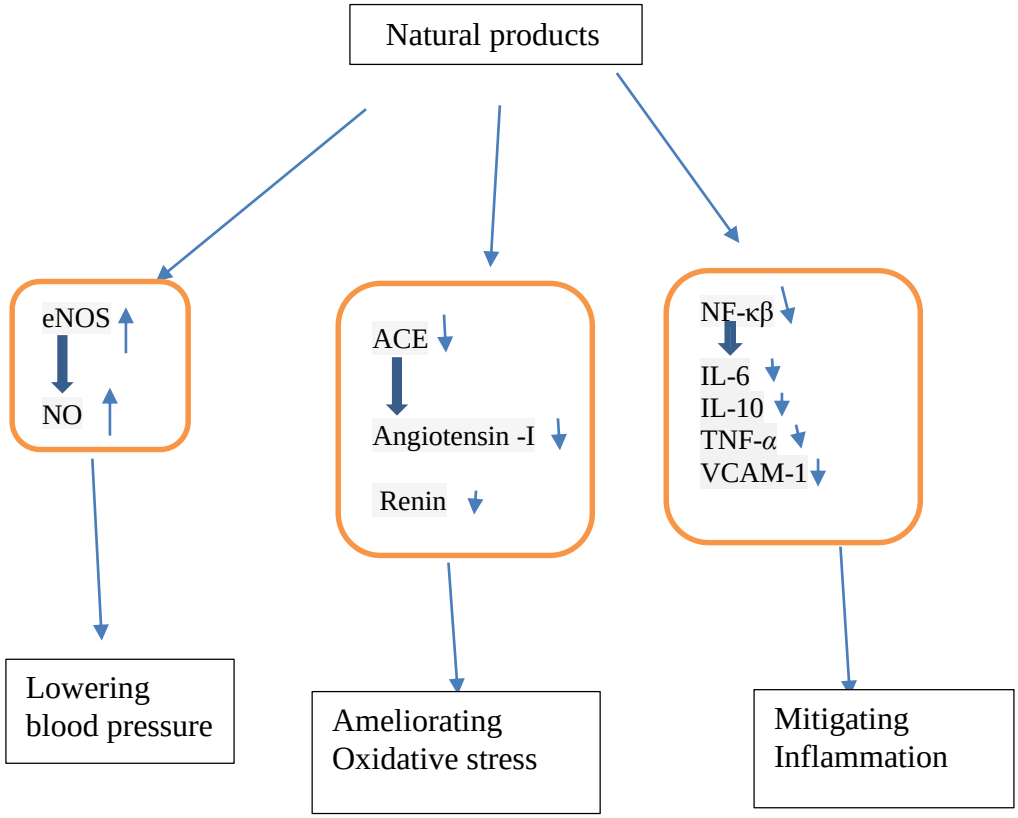

Figure 1: The relevant mechanisms of some antioxidant natural products and their bioactive compounds on CVDs

6.2.2 Discussion

In the paragraphs that follow, we'll talk about how natural remedies work to alleviate circulatory issues. Natural substances have the ability to lower blood pressure by lowering the hormones renin and angiotensin-1 as well as the activity of the ACE. All of these advantages are available right away. These drugs may increase the synthesis of nitric oxide (NO) and the activity of eNOS in addition to decreasing blood pressure. By using organic materials, oxidative stress's negative consequences may be lessened. This is done by upregulating the production of antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), and glutathione peroxidase (GPx), while downregulating the production of oxidative byproducts such malondialdehyde (MDA) and protein carbonyls (PC). Natural treatments may reduce inflammatory indicators such as tumour necrosis factor (TNF), interleukin-6 (IL-6), interleukin-

10 (IL-10), and vascular cell adhesion molecule-1 (VCAM-1) by activating the nuclear factor-kappa B (NF-) signalling pathway (Figure 1).

6.2.1.1 Reducing Blood Pressure

The link between heart disease and high blood pressure is well acknowledged [39]. For every 10 mm Hg decrease in systolic blood pressure, the likelihood of experiencing a major cardiovascular event was 50% lower in those with a history of the condition. It has been shown that a variety of medications may lower blood pressure and aid in the treatment and prevention of cardiovascular issues [40]. Nitric oxide (NO) production and RAS control were both responsible for the medications' hypotensive effects.

6.2.1.2 Regulating the Renin-Angiotensin System

The difficult and intricate process of maintaining normal blood pressure is aided by the RAS. To reduce RAS activity and blood pressure, renin and angiotensin-converting enzyme (ACE) synthesis may be suppressed [41–43]. Numerous randomised controlled trials have shown that RAS-blocking herbal medicines may reduce blood pressure. After consuming a hydrolysate of a winged bean seed, Sprague-Dawley (SD) rats showed dose-dependent decreases in blood pressure and ACE activity [44]. Several experiments have shown that a leaf extract from Solanum macrocarpon inhibits both the angiotensin-converting enzyme (ACE) and renin. After extract was administered to hypertensive rats, both heart rates and blood pressure reduced. The extract included the three essential polyphenols rutin, caffeine, and myricetin [45]. Similar studies have shown that ocimum sanctum and citrus paradisi infusions have hypotensive effects. Ocimum sanctum, which likewise suppressed the expression of the renin and angiotensinogen genes and decreased lipid and protein oxidation, increased the triglyceride accumulation in the kidneys of SD rats. These results further the body of knowledge [46] demonstrating the many interactions between Citrus paradisi and Ocimum sanctum that influence their hypotensive effects.

6.2.1.3 Increasing the Release of NO

The synthesis of nitric oxide (NO) by endothelial cells depends on endothelial nitric oxide synthase (eNOS). Nitric oxide (NO) may lower blood pressure by allowing the blood vessel walls to relax [47,48]. In order to boost NO production, blood pressure is reduced, and cardiovascular health is

protected. It's been shown that several naturally occurring compounds encourage the production of NO and have antihypertensive properties. It is thus almost impossible to avoid the advantages of lower blood pressure and a lower chance of developing heart disease. For instance, Morus alba decreased blood pressure in mice with wild-type blood vessels via triggering the relaxation of endothelial cells lining mesenteric arteries in response to nitric oxide (NO). Given that eNOS-deficient mice showed no hemodynamic effects, it is probable that Morus alba decreases blood pressure [49]. Rats with normal blood pressure and those who had spontaneously acquired hypertension both had a decrease in blood pressure after intravenous administration of white mulberry polysaccharides. On the other hand, in rats with normal blood pressure, the NO synthase inhibitor NG-nitro-L-arginine methyl ester (L-NAME) had a much less effect on lowering blood pressure. It was thought that nitric oxide was responsible for the hypotensive effects of the white mulberry fruit since the results from prior studies were consistent [50]. In hypertensive rats, sirtuin-1 and eNOS activity were enhanced, which boosted NO production and decreased blood pressure [51].

6.2.1.4 Ameliorating Oxidative Stress

In the face of oxidative stress, when antioxidant capacity is lowered, reactive oxygen species (ROS) are generated [52-54]. Protein carbonyls and malondialdehyde (MDA) are both peroxidative byproducts; they may be reduced by increasing the activity of antioxidant enzymes such catalase, superoxide dismutase (SOD), glutathione reductase (GR), and glutathione peroxidase (GPx). These natural substances have the potential to cure or prevent cardiovascular disease in the future. Both North American and Chinese wild rice significantly enhanced MDA, SOD activity, and total antioxidant capacity in hyperlipidemic rats, resulting in a decrease in oxidative stress. Two varieties of wild rice helped lower hyperlipidemia and inflammation in rats [55]. In order to reduce oxidative stress, both systolic and diastolic blood pressure were lowered and antioxidant defences were bolstered in Wistar rats. These benefits were seen after taking a polyphenol extract of Sambucus nigra L. Aliskiren, an antihypertensive medicine, was shown to have enhanced antioxidant properties and reduced negative effects when combined with other antioxidants [56]. Amounts of anthocyanins, phenolic acids, and flavonoids in dried chokeberry fruit extract were determined using high-performance liquid chromatography with diversity acid hydrazide (HPLC/DAD). Rats with spontaneously developing hypertension were used to analyse

the extract's results on lipid profiles, oxidative stress, and haemodynamic parameters. A significant reduction in both systolic and diastolic blood pressure was seen after administration of the anthocyanin-rich extract. The body's heightened need to urinate could explain this impact. Both erythrocyte and plasma levels of thiobarbituric acid reactive substances (TBARS) were significantly reduced in the treatment group. Despite decreased SOD activity in the treatment group compared to the control group, ferric ion-reducing antioxidant capacity (FRAP) increased after extract consumption. Although the fat and cholesterol content of the meal was substantial, along with the delicious cherry fruit and leaves, the Wistar rats did not gain weight. By increasing CAT, SOD, GPx, and GR activity and decreasing TBARS levels, liver function was enhanced and oxidative stress and inflammation were mitigated. Less fat was stored in the liver, and the serum lipid profiles improved. Potentially mitigating this impact is the blocking of genes involved in fatty acid production and oxidation [57]. Researchers have recently looked at the effects of a high-carb, high-fat diet on rats' oxidative stress, arterial stiffness, and vascular remodelling. Hydrolysate was shown to dramatically reduce hypertension, increased aortic pulse wave velocity, insulin resistance, dyslipidemia, hypertension, aortic wall hypertrophy, and vascular remodelling. Reducing TNF-alpha and adenosine deaminase in the blood was one of the effects of the hydrolysate. Superoxide production, plasma malondialdehyde (MDA), and other oxidative stress markers in vascular tissues were all reduced by the hydrolysate. The model group of rats had increased eNOS expression in their aortas, and their plasma levels of nitrate and nitrite were enhanced, suggesting that the hydrolysate may have stimulated NO production [58]. Saponins and phenolic compounds were among the 26 molecules found when HPLC-DAD-ESI-QTOF-MS/MS was applied to a root extract of Zygophyllum album. The extract had a significant impact on lowering oxidative stress, peroxidative damage to DNA and proteins, and the activities of SOD, CAT, and GPx. There was a similar boost in antioxidant power. Collagen deposition in the myocardium was averted, and plasmatic levels of pro-inflammatory cytokines were lowered thanks to the extract. Endothelial function and vascular oxidative stress have both been reported to increase after in vivo studies employing apple polyphenol extract [59].

6.2.1.5 Mitigating Inflammation

Inflammatory markers and cardiovascular disease have both been demonstrated to be linked to one another in studies [60, 61]. MCP-1 is a kind of chemoattractant protein, along with CRP, TNF-

alpha, IL-6, IL-10, VCAM-1, and IL-6. The possibility for pharmacological therapies to regulate the production of these cytokines has reduced the likelihood of acquiring cardiovascular disease. Markers of oxidative stress, apoptosis, and inflammation were all reduced by a Nepeta deflersiana ethanol extract, which meant less heart damage for Wistar rats. Nepeta deflersiana's anti-inflammatory and analgesic properties stem from the plant's ability to suppress the production of inflammatory mediators such tumour necrosis factor alpha (TNF-), interleukin 6 (IL-6), and interleukin 10 (IL-10). Zygophyllum album root extract has been shown to protect Wistar rat hearts by decreasing oxidative stress and inflammation. Zygophyllum album root extract reduces blood levels of inflammatory cytokines [62]. Blood inflammatory marker levels in male mice given a high-fat, high-fructose diet were perhaps significantly reduced by spinach nitrate [63]. Spinacia oleracea leaf methanol extract was used to reduce proinflammatory cytokine levels and prevent isoproterenol-induced cardiac necrosis in male Wistar rats [64]. The significant decrease in gene expression of TNF-, IL-6, VCAM-1, and MCP-1 provided evidence of the anti-inflammatory activities of the Antidesma bunius extract [65].

6.3 The effects of antioxidant natural products on cardiovascular disease

6.3.1. Result

Table 3: The effects of antioxidant natural products on cardiovascular disease

Plant types	Components	Study type	Subjects	Dose and time	Results	Ref.
Fruits						
Guava	NA	RCT	45 healthy students	400 g/day, 6 weeks	Reducing Blood Pressure, Total Cholesterol, Triglyceride, and Low Density Lipoprotein	[66]
Soursop	NA	RCT	143 hypertensive subjects	3 months	Reduced Blood Pressure	[67]

Orange juice	Hesperidin and naringin	Controlled nonrandomized clinical study	10 healthy women	300 mL/day, 2 months	Metabolism of LDL-C, blood sugar, insulin, and the gut flora are all enhanced.	[68]
Haskap berry	Anthocyanin	Cross-over study	20 adults aged 62-81 years	400 mg anthocyanins	Reducing blood pressure and enhancing short-term memory	[69]
Cherry juice	Anthocyanin	Pilot cross-over study	6 young and 7 old adults	300 mL or 100 mL, 3 times	Reduces blood pressure and heart rate	[70]
Pomegranate extract	Polyphenols	RCT	55 subjects without any symptomatic disease	Containing 210 mg punicalagins, 328 mg other pomegranate polyphenols, and 0-37 mg anthocyanins, 8 weeks	Reducing Blood Pressure	[71]
Plum juice	Anthocyanins	Pilot cross-over dose-timing study	12 older (65+ years) and 12 younger (18-45 years) adults	300 mL or 100 mL, 3 times	decreasing blood pressure and cardiovascular reactions	[72]
Noni and chokeberry juices	NA	RCT	88 young adults	Noni juice 30 mL; chokeberry juice 200 mL	Glucose (noni juice) and blood pressure (both systolic and diastolic) are lowered. DBP (chokeberry juice) somewhat reduced.	[73]
Vegetables						

Tomato extract	NA	RCT	65 patients with hypertension and a high risk of CVD	213 mg/day, 4 weeks	Reduced systolic and diastolic blood pressure and reduced mean arterial pressure	[74]
Beetroot juice	Nitrate	Open-label cross-over study	17 patients with chronic kidney disease	Containing 300 mg nitrate, 4 hours	reduced peripheral blood pressure and mean arterial pressure	[75]
Beetroot juice	Nitrate	Double-blind cross-over study	20 subjects with treated yet uncontrolled hypertension	Containing 12.9 mmol nitrate, 7 days	Reducing blood pressure and increasing plasma nitrite	[76]
Beetroot juice	Nitrate	Feasibility trial	40 hypertensive pregnant women	70 mL/day, 8 days	Reducing Blood Pressure	[77]
Sateria palmifolia	NA	Quasiexperiment	10 pregnant women	NA	Reducing Blood Pressure	[78]
Eggplant powder	NA	RCT	100 stressed participants with normal-high BP or stage 1 hypertension	1.2 g/day, 12 weeks	Improving BP and psychological state	[79]
Nuts						
Almond	NA	RCT	86 overweight or obese adults	15% energy from almond, 12 weeks	Bringing down blood pressure (BP) and abdominal fat	[80]

Walnuts	NA	RCT	100 overweight and obese participants	15% energy from walnut, 6 months	decreases in body fat, waist circumference, blood pressure, total cholesterol, and low-density lipoprotein (LDL)	[81]
Cashew nut	NA	RCT	300 Asian Indians with T2DM	30 g/day, 12 weeks	Decreasing SBP and increasing HDL-C	[82]
Mixed nuts	NA	RCT	48 overweight and obese adults	250 kcal, 4 and 8 weeks	Weight loss and glycemic control enhancement	[83]
Teas						
Green tea	Catechin	RCT	1,075 postmenopausal women	Containing 1,315 mg catechins, 6 and 12 months	Lowering TC, LDL-C, and non-HDL-C	[84]
Kosen-cha	Catechin	Open-label pilot study	6 obese subjects	5 g/L, 12 weeks	Lowering BW, BMI, waist circumferences, and serum TG levels and improving insulin resistance, vascular function, and cardiac hypertrophy	[85]
Goishi tea	Polyphenols	RCT	77 subjects	Containing 122 mg of polyphenols, 12 weeks	In order to improve cholesterol levels, HDL-C must be raised while TG are lowered.	[86]
Black tea	Phytosterol	RCT	Subjects with mild hypercholesterolemia	Phytosterol-enriched functional black tea, 4 weeks	Improving oxidative stress and lowering total cholesterol, low-density lipoprotein, and apolipoprotein B	[87]

6.3.2 Discussion

6.3.2.1 The Effects of Fruits on CVDs

Recent studies indicated that eating more fruits reduced the risk of cardiovascular disease. One research conclusion was this. Guava purée increased HDL cholesterol and decreased LDL, triglycerides, and total cholesterol [66]. Controlled experiments revealed this. After three months of therapy with 100 grams of sour sop fruit twice a day, the systolic, diastolic, and serum uric acid levels in the group decreased significantly. Despite eating the same quantity of sour sop fruit daily, this was true. Therapy lasted three months. Microbiome, LDL cholesterol, blood sugar, and insulin sensitivity were all enhanced in healthy women after two months of regular orange juice consumption (300 mL). Anthocyanin from haskap fruit (200 mg or 400 mg) successfully lowers blood pressure in individuals aged 62 to 81 [69]. Therefore, it is possible that consuming guava, soursop, and orange might aid in the management and prevention of cardiovascular disease.

6.3.2.2 The Effects of Vegetables on CVDs

Moreover, some veggies provided protection against cardiovascular diseases. A randomised controlled study [74] found that patients with hypertension and a higher risk of cardiovascular disease who took tomato extract (213 milligrammes daily) for four weeks saw improvements in their blood pressure and cardiovascular risk factors. Moreover, several studies demonstrated that beetroot's high nitrate concentration is responsible for its powerful hypotensive efficacy. In hypertensive pregnant women, for instance, 70 mL of beetroot juice was shown to substantially reduce DBP [76]. Eating 1.2 grams of eggplant powder daily has a significant impact on the health of those with high blood pressure or stage 1 hypertension [79]. Increasing one's consumption of tomatoes, beets, and eggplant is therefore recommended for the sake of arterial health.

6.3.2.3 The Effects of Nuts on CVDs

Many of the health advantages of nuts may be attributed to the antioxidants and phytochemicals they contain. Because they lower blood pressure and cholesterol, almonds have been demonstrated in several studies to be good for cardiovascular health. According to study [80], a 15% nut intake was linked to considerably lower systolic blood pressure, a smaller waist, and less overall body

fat. Weight, body mass index, waist size, diastolic blood pressure, total cholesterol, and low-density lipoprotein (LDL) cholesterol were all considerably lower after a 6-month randomized controlled experiment. When type 2 diabetic patients ingested more cashew nut products, their lipid profiles were better and they had a decreased chance of developing cardiovascular disease [82] than when they took a placebo. Throughout the course of the trial, we kept the same weight, blood pressure, cholesterol, and body mass index (BMI). Almonds, cashews, hazelnuts, pecans, Brazil nuts, macadamia nuts, pistachios, walnuts, peanuts, and slivered almonds are only a few foods that have been related to a decreased risk of cardiovascular disease [83].

6.3.2.4 The Effects of Teas on CVDs

After water, several investigations have been undertaken to establish whether tea has any health benefits. Several studies have found that tea consumption may lower coronary disease risk factors. Total cholesterol, low-density lipoprotein cholesterol, and non-HDL-C were all reduced in postmenopausal women who took green tea extract supplements [84]. Researchers found that hypercholesterolemia patients, regardless of severity, benefited by drinking functional black tea rich in phytosterols [87]. When oxidative stress decreased, both total and LDL cholesterol levels decreased. A preliminary open-label research also discovered that individuals who were fat and were administered 2 g/L kosen-cha everyday showed changes in insulin resistance, arterial function, and heart enlargement.

CHAPTER- 07

CONCLUSION

7.1 Conclusion

People all across the world have paid particular attention to cardiovascular problems since they are a major global health concern. Some naturally occurring antioxidant compounds have been demonstrated to provide defence against CVDs. Consuming antioxidant natural products has been linked to a lower incidence of cardiovascular disease events, according to several epidemiological research including participants of different ages, locations, and races. Several natural substances have been shown through experiments to have cardiovascular disease-preventing characteristics through regulating gut flora, lipid profiles, inflammation, and oxidative stress. Certain naturally occurring antioxidant molecules have recently been found to be helpful for treating and preventing cardiovascular disease. Many natural antioxidant products and the active ingredients in them have shown promise as dietary supplements or pharmaceuticals for the treatment and prevention of cardiovascular diseases. More research is required to determine the advantages of more natural antioxidants on CVDs as well as the efficacy of natural treatments for cardiovascular diseases. It also has to be made clear how the components work. Another important factor is the security of natural products and nutritious diets.

CHAPTER-8

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Project on A review on Potential therapeutic effect of antioxidant food components based on molecular mechanism in the treatment of Cardiovascular diseases A dissertation submitted to the Department of Pharmacy, Daffodil International University, slightly fulfils the needs for the Bachelor of Pharmacy degree (B. Pharm). Submitted To The Department of Pharmacy Faculty of Allied Health Sciences Daffodil International University In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy Submitted By Student ID: 191-29-1476 Batch: 21 Department of Pharmacy Faculty of Allied Health Sciences Daffodil International University April, 2022 i APPROVAL This project 'A review on Potential therapeutic effect of antioxidant food components based on molecular mechanism in the treatment of Cardiovascular diseases' submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents. Board of Examiners Professor Dr. Muniruddin Ahmed Head of the Department Department of Pharmacy Faculty of Allied Health Science Daffodil International University Internal Examiner 1 Internal Examiner 2 External Examine ii CERTIFICATION Dissertation Acceptance Form Daffodil International University, Department of Pharmacy. This is to certify

that the results of investigation of this project works are original & have not been submitted before in this University. This entire project work has been accepted satisfactory requirements for Bachelor of Pharmacy. Project Supervisor ..... Nazneen Ahmeda Sultana Assistant Professor Department of Pharmacy Faculty of Allied Health Sciences Daffodil International University iii Declaration I, with this, declare that I do this projectunder the supervision of Nazneen Ahmeda Sultana, Assistant Professor, Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, and reasonably meet the requirements of a Bachelor of Pharmacy (B. Pharm) degree. I declare that this project is entirely my creation. I further certify that the implementations in this project are unique and have never been submitted to any degree program at this university. Submitted By ..... Student ID: 191-29-1476 Batch: 21 Department of Pharmacy Faculty of Allied Health Sciences Daffodil International University iv Acknowledgement First and foremost, I would like to convey my heartfelt gratitude to the Almighty God for giving me the chance to study this subject, the capability to complete my project work, and finally the ability to write up the project work &results in order to fulfill the requirements for the Bachelor of Pharmacy degree. I would like to express my deepest appreciation and respect to my honorable supervisor Nazneen Ahmeda Sultana (Assistant Professor) Department of Pharmacy, Daffodil International University. I would also like to express my heartiest love to my friends who have supported me in my project work in the Laboratory and help to completing the project. I'd like to express my deepest greetings to Professor Dr. Muniruddin Ahamed, Professor and Head of the Pharmacy Department at Daffodil International University. I want to express my gratitude to everyone who has assisted me, directly or indirectly, in finishing my research, writing my dissertation, and bringing this project together. v My family, who has always supported and inspired me, as well as all of my esteemed instructors. vi Abstract Cardiovascular diseases (CVDs) have recently come to the forefront due to their alarmingly rising incidence and mortality rate. Epidemiological studies have revealed that those who eat a diet high in whole grains, fruits, vegetables, and nuts have a decreased chance of developing cardiovascular disease. Consuming a broad array of antioxidant natural products and the bioactive components of these substances greatly enhanced the cardiovascular health of the research participants. Puerarin may include high levels of antioxidants such polyphenols, polysaccharides, anthocyanins, epigallocatechin gallate, quercetin, rutin, and others. These results may arise from changes in blood pressure, lipid profiles, oxidative stress, inflammation, and maybe even the makeup of gut flora. Numerous studies have indicated that eating antioxidant-rich foods including soursop, beetroot, garlic, almonds, and green tea improves cardiovascular health. With a focus on clarifying underlying processes and reporting clinical trials, we collated data from epidemiological, experimental, and clinical studies evaluating the effect of diverse antioxidant natural products and their bioactive components on cardiovascular disorders. vii Contents CHAPTER -01 ..... 1 INTRODUCTION ..... 1 1. Introduction..... 2 CHAPTER- 02 ..... 3 GOAL OF MY STUDY ..... 3 2.1 Goal of My Study..... 4 CHAPTER- 03 ..... 5 METHODOLGY..... 5 3.1 Methodology ..... 6 3.2. Introduction..... 6 3.3. Research Design ..... 6 3.4. Method of Data Analysis ..... 6 3.5. 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Results and Discussion ..... 14 6.2.1.1 Reducing Blood Pressure ..... 17 6.2.1.3 Increasing the Release of NO ..... 17 6.2.1.4 Ameliorating Oxidative Stress ..... 18 6.2.1.5 Mitigating Inflammation ..... 19 6.3 The effects of antioxidant natural products on cardiovascular disease..... 20 6.3.2.1 The Effects of Fruits on CVDs ..... 24 6.3.2.2 The Effects of Vegetables on CVDs ..... 24 6.3.2.3 The Effects of Nuts on CVDs ..... 24 6.3.2.4 The Effects of Teas on CVDs ..... 25 CHAPTER- 07 ..... 26 CONCLUSION..... 26 7.1 Conclusion ..... 27 viii CHAPTER-8 ..... 28 REFERENCE ..... 28 8.1 Reference ..... 29 List of figure Figure 1: The relevant mechanisms of some antioxidant natural products and their bioactive compounds on CVDs .....16 List of table Table 1: Epidemiological studies .....8 Table 2: The effects of antioxidant natural products on CVDs from experimental studies.... 14-15 Table 3: The effects of antioxidant natural products on CVDs ..... 20-23 ix CHAPTER -01 INTRODUCTION 1. Introduction According to the World Health Organisation (WHO), 25 percent of all deaths worldwide are caused by cardiovascular disease [1]. The phrase "cardiovascular disease" (CVD) refers to a group of conditions that includes heart failure, stroke, excessive blood pressure, and coronary heart disease (CHD). The occurrence of cardiovascular disease has been linked to a wide range of factors [2, 3]. This category of diseases includes oxidative stress, intestinal dysbiosis, dyslipidemia, hypertension, and atherosclerosis. Synthetic medications used to treat cardiovascular diseases are associated with a wide variety of undesired side effects [5, 6], including hyperkalemia, arrhythmias, and gastrointestinal issues. These are only few of the many possible negative reactions. However, there is mounting evidence that natural antioxidants may be utilised safely and effectively in the management of cardiovascular diseases [7–11]. Numerous illnesses and ailments, such as obesity, cancer, inflammation, liver damage, and cardiovascular disease, have been linked to a reduction in natural product consumption. In addition to all of these advantages, they are also a good source of essential nutrients such fibre, flavonoids, vitamins, and minerals [12-15]. Fruits, vegetables, teas, cereals, and nuts are all good sources of antioxidants, and eating them regularly has been shown in epidemiological studies to significantly lower the risk of cardiovascular disease [16,17]. Many research [18–20] have shown the efficacy of certain antioxidant natural products and their active components in the treatment and prevention of CVDs. Several naturally occurring antioxidant molecules have been found to be useful in the treatment and prevention of cardiovascular disorders in human clinical investigations [21]. This review aims to synthesise the results of epidemiological, experimental, and clinical investigations conducted over the last decade on the impact of a specific class of naturally occurring antioxidants and the bioactive components of those antioxidants on cardiovascular diseases. The study's major emphasis was on the clinical application of these medicines. CHAPTER- 02 GOAL OF MY STUDY 2.1 Goal of My Study The goal

of the study is: ? To know about the antioxidant food component products. ? To know about source of natural antioxidant. ? To learn which type of plants contains antioxidant activity. ? To find out natural antioxidant mechanism for cardiovascular disease. ? To ascertain the diagnosis and natural treatment options of cardiovascular disease. ? To understand more about cardiovascular risk factor. CHAPTER- 03 METHODOLGY 3.1 Methodology 3.2. Introduction The examination is preceded with a literature study. For this study, 50 or so publications are reviewed. 3.3. Research Design This exploration was planned through Google scholar, PubMed and many other websites to find literature. For referencing mendeley software was used. 3.4. Method of Data Analysis After gathering a variety of data, each piece was examined for accuracy and internal coherence to rule out any missing or inconsistent pieces, and those were then deleted. Information research was carried out using Microsoft's dominant updated version. All data was gathered between 2012 and 2022. 3.5. Ethical Considerations The members of the investigation were spoken to and given the go-ahead verbally for the information gathering process. The respondents' identities were kept secret, and participants in the study were informed that they may drop out at any point during the information gathering process. The study was sponsored by the Department of Pharmacy. CHAPTER- 04 Epidemiology 4.1 Epidemiology Table 1: Epidemiological studies Plants Study type Subjects Results Reference Fruit A cross-sectional analysis 1,590 adults In the 50-59 age group, less fruit consumption was linked to higher blood pressure (PR: 1.62; 95% CI, 1.09-2.41). [22] Fruit Cohort analysis 70,047 Chinese adults with CVD or hypertension correlated negatively with death from cardiovascular disease (HR = 0.79; 95% CI = 0.73-0.86). [23] Vegetable A Cross- sectional analysis 18,757 adolescents Risk of hypertension was reduced (OR, 0.74; 95% CI, 0.58-0.94) among those who ate at least three servings of vegetables each day. [24] Allium vegetable Cohort analysis Adult men and women Risk of CVD events reduced by 64% (HR: 0.36; 95% CI: 0.18-0.71) [25] Nut 3 significant cohort analysis 34,103 men 77,815 women 80,737 women linked negatively to CHD (RR 0.94, 95% CI 0.89-0.99), stroke (RR 0.89, 95% CI 0.83-0.95), and CVD (RR 0.92, 95% CI 0.86-0.98). [26] Fruit, vegetable A Cross- sectional analysis 1,596 adolescents and young people in Tanzania and Uganda Reduces hypertension risk (OR = 0.7; 95% CI = 0.50-0.98). [27] Fruit, vegetable A Cross- sectional analysis 229 patients with primary hypertension The reduction of blood pressure, heart rate, and body mass index [28] Many epidemiological studies have shown that plant-based diets can prevent and even treat cardiovascular disease. Researchers in China found that among 18,757 young adults, the risk of developing hypertension was reduced among those who had three or more servings of vegetables daily [24]. Fist sizes in the male gender tend to be around the same as a single serve. This investigation was carried out by Chinese researchers. Several cohort studies have found that those who eat a plant-based diet had a lower chance of developing cardiovascular disease. There was a significant difference in the systolic blood pressure (SBP) and blood glucose levels of 521,891 Chinese adults aged 30-79 who ate fresh fruit on a regular basis and those who did not. This was evident when comparing consistent usage to less frequent usage or no usage at all, as predicted. Between 0.75 and 0.79 was the risk ratio for an ischemic stroke, whereas it was between 0.52 and 0.74 for a hemorrhagic stroke, 0.66 and 0.75 for an incident major coronary event, and between 0.50 and 0.67 for mortality due to cardiovascular disease. [26]. Eating allium plants like garlic and onion was linked to a 64% decrease in cardiovascular disease outcomes (HR= 0.36; 95% CI: 0.18- 0.71) [27] in a different experiment with 3,052 individuals. In a study of young individuals in the Mediterranean, the Human Relative Hazard (95% Confidence Interval) for those in the highest quintiles of fruit and whole grain eating was 0.51 [0.27-0.95], and for those in the highest quintiles of whole grain consumption, it was 0.43 [0.20-0.93]. According to a second prospective study involving 2,295 Iranians, individuals who consumed the most dietary fibre from fruits, vegetables, cereals, legumes, nuts, and other sources had a decreased risk of cardiovascular disease than those who consumed the least. The hazard ratios (HR) for cardiovascular disease were 0.90 (0.44-1.86), 0.31 (0.15-0.52), 0.49 (0.24-1.02), and 0.44 (0.22-0.89), in that order. However, a cohort study found a significantly decreased risk of cardiovascular disease associated with nut consumption [28]. It is unclear if the advantage of nuts in lowering the risk of cardiovascular disease (CVD) is due to the nuts themselves or the bioactive elements they contain, such as dietary fibre. Emerging data from epidemiological studies suggests that these products' bioactive components and some naturally occurring antioxidant compounds may work as a defence against cardiovascular disease (CVD). However, there is no guarantee of the results. Fresh vegetables, cereals, legumes, nuts, and other plant-based diets have all been linked to a reduced risk of cardiovascular diseases (CVDs). Many different plants may offer defence against cardiovascular diseases, according to growing body of scientific research. Because there is an inverse correlation between the risk of cardiovascular disease and consumption of such foods, avoiding plant-based meals can reduce a person's likelihood of getting the condition. CHAPTER -05 Literature review 5.1 Dietary fruits and vegetables and cardiovascular diseases risk. Critical reviews in food science and nutrition. [29]. The majority of the topics discussed in the article relate to bioactive compounds, food, heart disease, diabetes, obesity, and diseases including hypertension and hypertension. We examine the data supporting the idea that a diet rich in fruits and vegetables reduces the risk of cardiovascular disease in this article. Eating a diet high in fruits and vegetables may help lower the prevalence of cardiovascular disease (CVD), according to early data from observational studies. Ongoing discussion surrounds the recommended amount of meals, which may not be five, as well as their possible impacts. It is impossible to show via the use of randomised controlled trials that a diet rich in fruits and vegetables protects cardiovascular disease. Due to their high energy content, low glycemic load, and other bioactive nutritional benefits, fruits and vegetables can be used as a preventative approach. In order to reduce the risk of CVD, dietary patterns and consuming whole meals may be more important to focus on than specific nutrients, according to a recent study, considering the complicated interplay between various nutrients and possibly genetic risk factors. A fuller knowledge of the link between eating fruits and vegetables and cardiovascular risk would be very beneficial for health professionals in order to properly focus clinical practises and public health [29]. 5.2 Food antioxidants and their anti-inflammatory properties: a potential role in cardiovascular diseases and cancer prevention. Diseases. [30]. This study looks at the connections between stress, inflammation, transcription factors, the microbiome, vitamins, pro-oxidants, flavonoids, and carotenoids. Numerous studies from the past indicate that adopting a Mediterranean-style diet has a significant detrimental effect on the incidence of cardiovascular illnesses (CVDs). According to a study that examined how diet impacted the oxidation of lipoproteins, people who followed the Mediterranean diet and used virgin olive oil experienced much lower levels of oxidative stress than those who ate low-fat meals. There has been much research into the mechanisms behind the interventional stimulation of apoptosis, the effects of these processes on cancer and cardiovascular disease, the inhibition of proliferation, inflammation, invasion, and metastasis, as well as the activation of apoptosis. Fruits, vegetables, tea, and wine all contain flavonoid antioxidants, which are compounds having 2- or 3- phenylchroman structures. It has been proven that these compounds aid in the prevention of heart disease and cancer. Flavonoids like luteolin, quercetin, kaempferol, myricetin, and apigenin are among them. Flavonoids can defend DNA against hydroxyl radical damage through the crucial chelation step. In the hopes that they will one day be a successful substitute for conventional pharmaceutical therapies, the primary and secondary human metabolomes have been explored [30]. 5.3 Antioxidant food components for the prevention and treatment of cardiovascular diseases: effects, mechanisms, and clinical studies. Oxidative medicine and cellular longevity. [31]. The results of this study indicate that increasing the intake of fruits, vegetables, nuts, and cereals may reduce the prevalence of cardiovascular diseases (CVDs), with the antioxidants included in these foods serving as the main protective element. The objective of this article is to summarise the results of epidemiological, experimental, and clinical research on cardiovascular diseases (CVDs) conducted over the past five years looking at the effects of various antioxidant natural products and their bioactive components. On clinical trials and how they work, there will be a lot of emphasis. This study also shows that a variety of naturally occurring foods, like fruits, vegetables, and nuts, have antioxidant properties that can lower blood pressure, inflammation, RAS, boost nitric oxide levels, improve lipid profiles, and lower the risk of cardiovascular disease. When 45 healthy students consume 400 grammes of guava daily, blood pressure, triglycerides, and LDL cholesterol levels decrease. Some individuals, including men, women, and the elderly, are advised to consume meals that contain vegetables, tomato extract, and carrot juice in order to reduce their chance of developing cardiovascular disease [31]. CHAPTER -06 Result & Discussion 6. Results and Discussion 6.1. The effects of antioxidant natural products on CVDs from experimental studies 6.1.1. Result Table 2: The effects of antioxidant natural

products on CVDs from experimental studies. Plants Components Study type Effects and mechanisms Reference Winged bean seed Peptide In vitro In vivo Blocking ACE Enzyme Activity reduction in blood pressure [32] Solanum macrocarpon Polyphenols In vitro In vivo Reducing the production of ACE and renin Reduced blood pressure and heart rate [33] Pigeon pea Protein In vitro In vivo blocking ACE and renin enzymes and mopping up free radicals reduction in blood pressure [34] Tea Polyphenols In vivo Reducing total and low- density lipoprotein cholesterol and plaque area/lumen area [35] White mulberry fruit Polysaccharides In vitro In vivo Relaxation of the endothelium and release of [36] nitric oxide in the arteries of the rat mesenteric gland. Decreases in systolic and diastolic blood Rice bran Protein In vivo Reducing Blood Pressure (ACE↓, NO, and eNOS↑) [37] Lycium ruthenicum Murray Anthocyanins In vivo Enhanced resistance to oxidative stress and inflammation [38] 6.1.2 Discussion By simulating the enzyme as a peptide and the plant as a bean seed, this table demonstrates that lowering ACE enzyme activity lowers blood pressure in both in vitro and in vivo tests. On bean seeds, in vitro research was done. Through research carried out under both vitro and in vivo circumstances, it has been demonstrated that the polyphenolic component of Solanum macrocarpon can lower blood pressure and heart rate. The reduction of total cholesterol, low- density lipoprotein cholesterol, and plaque area by tea plant extracts has been demonstrated in studies on living animals. Increased resilience to oxidative and inflammatory stress is seen in plants from the Lyceum ruthenium Murray genus. According to this study, eating a few certain plant species can lower your chance of developing cardiovascular problems. 6.2. The relevant mechanisms of some antioxidant natural products and their bioactive compounds on CVDs 6.2.1. Result Natural products eNOS ACE NO Angiotensin -I Renin NF-κβ IL-6 IL-10 TNF-α VCAM-1 Lowering blood pressure Ameliorating Mitigating Oxidative stress Inflammation Figure 1: The relevant mechanisms of some antioxidant natural products and their bioactive compounds on CVDs 6.2.2 Discussion In the paragraphs that follow, we'll talk about how natural remedies work to alleviate circulatory issues. Natural substances have the ability to lower blood pressure by lowering the hormones renin and angiotensin-1 as well as the activity of the ACE. All of these advantages are available right away. These drugs may increase the synthesis of nitric oxide (NO) and the activity of eNOS in addition to decreasing blood pressure. By using organic materials, oxidative stress's negative consequences may be lessened. This is done by upregulating the production of antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), and glutathione peroxidase (GPx), while downregulating the production of oxidative byproducts such malondialdehyde (MDA) and protein carbonyls (PC). Natural treatments may reduce inflammatory indicators such as tumour necrosis factor (TNF), interleukin-6 (IL-6), interleukin- 10 (IL-10), and vascular cell adhesion molecule-1 (VCAM-1) by activating the nuclear factor-kappa B (NF-) signalling pathway (Figure 1). 6.2.1.1 Reducing Blood Pressure The link between heart disease and high blood pressure is well acknowledged [39]. For every 10 mm Hg decrease in systolic blood pressure, the likelihood of experiencing a major cardiovascular event was 50% lower in those with a history of the condition. It has been shown that a variety of medications may lower blood pressure and aid in the treatment and prevention of cardiovascular issues [40]. Nitric oxide (NO) production and RAS control were both responsible for the medications' hypotensive effects. 6.2.1.2 Regulating the Renin-Angiotensin System The difficult and intricate process of maintaining normal blood pressure is aided by the RAS. To reduce RAS activity and blood pressure, renin and angiotensin-converting enzyme (ACE) synthesis may be suppressed [41–43]. Numerous randomised controlled trials have shown that RAS-blocking herbal medicines may reduce blood pressure. After consuming a hydrolysate of a winged bean seed, Sprague-Dawley (SD) rats showed dose-dependent decreases in blood pressure and ACE activity [44]. Several experiments have shown that a leaf extract from Solanum macrocarpon inhibits both the angiotensin-converting enzyme (ACE) and renin. After extract was administered to hypertensive rats, both heart rates and blood pressure reduced. The extract included the three essential polyphenols rutin, caffeine, and myricetin [45]. Similar studies have shown that ocimum sanctum and citrus paradisi infusions have hypotensive effects. Ocimum sanctum, which likewise suppressed the expression of the renin and angiotensinogen genes and decreased lipid and protein oxidation, increased the triglyceride accumulation in the kidneys of SD rats. These results further the body of knowledge [46] demonstrating the many interactions between Citrus paradisi and Ocimum sanctum that influence their hypotensive effects. 6.2.1.3 Increasing the Release of NO The synthesis of nitric oxide (NO) by endothelial cells depends on endothelial nitric oxide synthase (eNOS). Nitric oxide (NO) may lower blood pressure by allowing the blood vessel walls to relax [47,48]. In order to boost NO production, blood pressure is reduced, and cardiovascular health is protected. It's been shown that several naturally occurring compounds encourage the production of NO and have antihypertensive properties. It is thus almost impossible to avoid the advantages of lower blood pressure and a lower chance of developing heart disease. For instance, Morus alba decreased blood pressure in mice with wild-type blood vessels via triggering the relaxation of endothelial cells lining mesenteric arteries in response to nitric oxide (NO). Given that eNOS- deficient mice showed no hemodynamic effects, it is probable that Morus alba decreases blood pressure [49]. Rats with normal blood pressure and those who had spontaneously acquired hypertension both had a decrease in blood pressure after intravenous administration of white mulberry polysaccharides. On the other hand, in rats with normal blood pressure, the NO synthase inhibitor NG-nitro-L-arginine methyl ester (L-NAME) had a much less effect on lowering blood pressure. It was thought that nitric oxide was responsible for the hypotensive effects of the white mulberry fruit since the results from prior studies were consistent [50]. In hypertensive rats, sirtuin- 1 and eNOS activity were enhanced, which boosted NO production and decreased blood pressure [51]. 6.2.1.4 Ameliorating Oxidative Stress In the face of oxidative stress, when antioxidant capacity is lowered, reactive oxygen species (ROS) are generated [52-54]. Protein carbonyls and malondialdehyde (MDA) are both peroxidative byproducts; they may be reduced by increasing the activity of antioxidant enzymes such catalase, superoxide dismutase (SOD), glutathione reductase (GR), and glutathione peroxidase (GPx). These natural substances have the potential to cure or prevent cardiovascular disease in the future. Both North American and Chinese wild rice significantly enhanced MDA, SOD activity, and total antioxidant capacity in hyperlipidemic rats, resulting in a decrease in oxidative stress. Two varieties of wild rice helped lower hyperlipidemia and inflammation in rats [55]. In order to reduce oxidative stress, both systolic and diastolic blood pressure were lowered and antioxidant defences were bolstered in Wistar rats. These benefits were seen after taking a polyphenol extract of Sambucus nigra L. Aliskiren, an antihypertensive medicine, was shown to have enhanced antioxidant properties and reduced negative effects when combined with other antioxidants [56]. Amounts of anthocyanins, phenolic acids, and flavonoids in dried chokeberry fruit extract were determined using high-performance liquid chromatography with diversity acid hydrazide (HPLC/DAD). Rats with spontaneously developing hypertension were used to analyse 18 ©Daffodil International University the extract's results on lipid profiles, oxidative stress, and haemodynamic parameters. A significant reduction in both systolic and diastolic blood pressure was seen after administration of the anthocyanin-rich extract. The body's heightened need to urinate could explain this impact. Both erythrocyte and plasma levels of thiobarbituric acid reactive substances (TBARS) were significantly reduced in the treatment group. Despite decreased SOD activity in the treatment group compared to the control group, ferric ion-reducing antioxidant capacity (FRAP) increased after extract consumption. Although the fat and cholesterol content of the meal was substantial, along with the delicious cherry fruit and leaves, the Wistar rats did not gain weight. By increasing CAT, SOD, GPx, and GR activity and decreasing TBARS levels, liver function was enhanced and oxidative stress and inflammation were mitigated. Less fat was stored in the liver, and the serum lipid profiles improved. Potentially mitigating this impact is the blocking of genes involved in fatty acid production and oxidation [57]. Researchers have recently looked at the effects of a high-carb, high-fat diet on rats' oxidative stress, arterial stiffness, and vascular remodelling. Hydrolysate was shown to dramatically reduce hypertension, increased aortic pulse wave velocity, insulin resistance, dyslipidemia, hypertension, aortic wall hypertrophy, and vascular remodelling. Reducing TNF-alpha and adenosine deaminase in the blood was one of the effects of the hydrolysate. Superoxide production, plasma malondialdehyde (MDA), and other oxidative stress markers in vascular tissues were all reduced by the hydrolysate. The model group of rats had increased eNOS expression in their aortas, and their plasma levels of nitrate and nitrite were enhanced, suggesting that the hydrolysate may have stimulated NO production [58]. Saponins and phenolic compounds were among the 26 molecules found when HPLC-DAD-ESI-QTOF-MS/MS was applied to a root extract of Zygophyllum album. The extract had a significant impact on lowering oxidative stress, peroxidative damage to DNA and proteins, and the activities of

SOD, CAT, and GPx. There was a similar boost in antioxidant power. Collagen deposition in the myocardium was averted, and plasmatic levels of pro-inflammatory cytokines were lowered thanks to the extract. Endothelial function and vascular oxidative stress have both been reported to increase after in vivo studies employing apple polyphenol extract [59]. 6.2.1.5 Mitigating Inflammation Inflammatory markers and cardiovascular disease have both been demonstrated to be linked to one another in studies [60, 61]. MCP-1 is a kind of chemoattractant protein, along with CRP, TNF- alpha, IL-6, IL-10, VCAM-1, and IL-6. The possibility for pharmacological therapies to regulate the production of these cytokines has reduced the likelihood of acquiring cardiovascular disease. Markers of oxidative stress, apoptosis, and inflammation were all reduced by a Nepeta deflersiana ethanol extract, which meant less heart damage for Wistar rats. Nepeta deflersiana's anti- inflammatory and analgesic properties stem from the plant's ability to suppress the production of inflammatory mediators such tumour necrosis factor alpha (TNF-), interleukin 6 (IL-6), and interleukin 10 (IL-10). Zygophyllum album root extract has been shown to protect Wistar rat hearts by decreasing oxidative stress and inflammation. Zygophyllum album root extract reduces blood levels of inflammatory cytokines [62]. Blood inflammatory marker levels in male mice given a high-fat, high-fructose diet were perhaps significantly reduced by spinach nitrate [63]. Spinacia oleracea leaf methanol extract was used to reduce proinflammatory cytokine levels and prevent isoproterenol-induced cardiac necrosis in male Wistar rats [64]. The significant decrease in gene expression of TNF-, IL-6, VCAM-1, and MCP-1 provided evidence of the anti- inflammatory activities of the Antidesma bunius extract [65]. 6.3 The effects of antioxidant natural products on cardiovascular disease 6.3.1. Result Table 3: The effects of antioxidant natural products on cardiovascular disease Plant types Componen Study ts type Subjects Dose and Results time Ref. Fruits Guava NA RCT 45 healthy students 400 g/day, 6 weeks Reducing Blood Pressure, Total Cholesterol, Triglyceride, and Low Density Lipoprotein [66] Soursop NA RCT 143 hypertensi ve subjects 3 months Reduced Blood Pressure [67] Orange juice Hesperidin and naringin Controlle d nonrando mized clinical study 10 healthy women 300 mL/day, 2 months Metabolism of LDL-C, blood sugar, insulin, and the gut flora are all enhanced. [68] Haskap berry Anthocyani n Cross- over study 20 adults aged 62-81 years 400 mg anthocyanin s Reducing blood pressure and enhancing short- term memory [69] Cherry juice Anthocyani n Pilot cross-over study 6 young and 7 old adults 300 mL or 100 mL, 3 times Reduces blood pressure and heart rate [70] Pomegran ate extract Polyphenol s RCT 55 subjects without any symptomat ic disease Containing 210 mg punicalagins , 328 mg other pomegranate polyphenols, and 0-37 mg anthocyanin s, 8 weeks Reducing Blood Pressure [71] Plum juice Anthocyani ns Pilot cross-over dose- timing study 12 older (65+ years) and 12 younger (18-45 years) adults 300 mL or 100 mL, 3 times decreasing blood pressure and cardiovascular reactions [72] Noni and chokeberr y juices NA RCT 88 young adults Noni juice 30 mL; chokeberry juice 200 mL Glucose (noni juice) and blood pressure (both systolic and diastolic) are lowered. DBP (chokeberry juice) somewhat reduced. [73] Vegetables Tomato extract NA RCT 65 patients with hypertensi on and a high risk of CVD 213 mg/day, 4 weeks Reduced systolic and diastolic blood pressure and reduced mean arterial pressure [74] Beetroot juice Nitrate Open- label cross-over study 17 patients with chronic kidney disease Containing 300 mg nitrate, 4 hours reduced peripheral blood pressure and mean arterial pressure [75] Beetroot juice Nitrate Double- blind cross-over study 20 subjects with treated yet uncontroll ed hypertensi on Containing 12.9 mmol nitrate, 7 days Reducing blood pressure and increasing plasma nitrite [76] Beetroot juice Nitrate Feasibilit y trial 40 hypertensi ve pregnant women 70 mL/day, 8 days Reducing Blood Pressure [77] Sateria palmifolia NA Quasiexp eriment 10 pregnant women NA Reducing Blood Pressure [78] Eggplant powder NA RCT 100 stressed participant s with normal- high BP or stage 1 hypertensi on 1.2 g/day, 12 weeks Improving BP and psychological state [79] Nuts Almond NA RCT 86 overweight or obese adults 15% energy from almond, 12 weeks Bringing down blood pressure (BP) and abdominal fat [80] Walnuts NA RCT 100 overweight and obese participant s 15% energy from walnut, 6 months decreases in body fat, waist circumference, blood pressure, total cholesterol, and low-density lipoprotein (LDL) [81] Cashew nut NA RCT 300 Asian Indians with T2DM 30 g/day, 12 weeks Decreasing SBP and increasing HDL-C [82] Mixed nuts NA RCT 48 overweight and obese adults 250 kcal, 4 and 8 weeks Weight loss and glycemic control enhancement [83] Teas Green tea Catechin RCT 1,075 postmenop ausal women Containing 1,315 mg catechins, 6 and 12 months Lowering TC, LDL-C, and non- HDL-C [84] Kosen- cha Catechin Open- label pilot study 6 obese subjects 5 g/L, 12 weeks Lowering BW, BMI, waist circumferences, and serum TG levels and improving insulin resistance, vascular function, and cardiac hypertrophy [85] Goishi tea Polyphenol s RCT 77 subjects Containing 122 mg of polyphenols, 12 weeks In order to improve cholesterol levels, HDL-C must be raised while TG are lowered. [86] Black tea Phytosterol RCT Subjects with mild hyperchole sterolemia Phytosterol-enriched functional black tea, 4 weeks Improving oxidative stress and lowering total cholesterol, low- density lipoprotein, and apolipoprotein B [87] 6.3.2 Discussion 6.3.2.1 The Effects of Fruits on CVDs Recent studies indicated that eating more fruits reduced the risk of cardiovascular disease. One research conclusion was this. Guava purée increased HDL cholesterol and decreased LDL, triglycerides, and total cholesterol [66]. Controlled experiments revealed this. After three months of therapy with 100 grams of sour sop fruit twice a day, the systolic, diastolic, and serum uric acid levels in the group decreased significantly. Despite eating the same quantity of sour sop fruit daily, this was true. Therapy lasted three months. Microbiome, LDL cholesterol, blood sugar, and insulin sensitivity were all enhanced in healthy women after two months of regular orange juice consumption (300 mL). Anthocyanin from haskap fruit (200 mg or 400 mg) successfully lowers blood pressure in individuals aged 62 to 81 [69]. Therefore, it is possible that consuming guava, soursop, and orange might aid in the management and prevention of cardiovascular disease. 6.3.2.2 The Effects of Vegetables on CVDs Moreover, some veggies provided protection against cardiovascular diseases. A randomised controlled study [74] found that patients with hypertension and a higher risk of cardiovascular disease who took tomato extract (213 milligrammes daily) for four weeks saw improvements in their blood pressure and cardiovascular risk factors. Moreover, several studies demonstrated that beetroot's high nitrate concentration is responsible for its powerful hypotensive efficacy. In hypertensive pregnant women, for instance, 70 mL of beetroot juice was shown to substantially reduce DBP [76]. Eating 1.2 grams of eggplant powder daily has a significant impact on the health of those with high blood pressure or stage 1 hypertension [79]. Increasing one's consumption of tomatoes, beets, and eggplant is therefore recommended for the sake of arterial health. 6.3.2.3 The Effects of Nuts on CVDs Many of the health advantages of nuts may be attributed to the antioxidants and phytochemicals they contain. Because they lower blood pressure and cholesterol, almonds have been demonstrated in several studies to be good for cardiovascular health. According to study [80], a 15% nut intake was linked to considerably lower systolic blood pressure, a smaller waist, and less overall body fat. Weight, body mass index, waist size, diastolic blood pressure, total cholesterol, and low- density lipoprotein (LDL) cholesterol were all considerably lower after a 6-month randomized controlled experiment. When type 2 diabetic patients ingested more cashew nut products, their lipid profiles were better and they had a decreased chance of developing cardiovascular disease [82] than when they took a placebo. Throughout the course of the trial, we kept the same weight, blood pressure, cholesterol, and body mass index (BMI). Almonds, cashews, hazelnuts, pecans, Brazil nuts, macadamia nuts, pistachios, walnuts, peanuts, and slivered almonds are only a few foods that have been related to a decreased risk of cardiovascular disease [83]. 6.3.2.4 The Effects of Teas on CVDs After water, several investigations have been undertaken to establish whether tea has any health benefits. Several studies have found that tea consumption may lower coronary disease risk factors. Total cholesterol, low-density lipoprotein cholesterol, and non-HDL-C were all reduced in postmenopausal women who took green tea extract supplements [84]. Researchers found that hypercholesterolemia patients, regardless of severity, benefited by drinking functional black tea rich in phytosterols [87]. When oxidative stress decreased, both total and LDL cholesterol levels decreased. A preliminary open-label research also discovered that individuals who were fat and were administered 2 g/L kosen-cha everyday showed changes in insulin resistance, arterial function, and heart enlargement. CHAPTER- 07 CONCLUSION 7.1 Conclusion People all across the world have paid particular attention to cardiovascular problems since they are a major global health concern. Some naturally occurring antioxidant compounds have been demonstrated to provide defence against CVDs. Consuming antioxidant natural products has been linked to a lower incidence of cardiovascular disease events, according to several epidemiological research including participants of different ages, locations, and races. Several natural substances have been shown through experiments to have cardiovascular disease-preventing characteristics through regulating gut flora, lipid profiles, inflammation, and oxidative stress. Certain naturally

occurring antioxidant molecules have recently been found to be helpful for treating and preventing cardiovascular disease. Many natural antioxidant products and the active ingredients in them have shown promise as dietary supplements or pharmaceuticals for the treatment and prevention of cardiovascular diseases. More research is required to determine the advantages of more natural antioxidants on CVDs as well as the efficacy of natural treatments for cardiovascular diseases. It also has to be made clear how the components work. Another important factor is the security of natural products and nutritious diets. CHAPTER-8 REFERENCE 8.1 Reference 1. Wang H, Naghavi M, Allen C, Barber RM, Bhutta ZA, Carter A, Casey DC, Charlson FJ, Chen AZ, Coates MM, Coggeshall M. Global, regional, and national life expectancy, all- cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. 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