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Study on the Antioxidative Property of *Dandelion (Taraxacum officinale)* Polysaccharides on Atherosclerosis

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ABSTRACT

Dandelion (Taraxacum officinale) is a member of the Asteraceae family, a traditional natural medicinal plant. The antioxidant property of dandelion polysaccharides can alleviate atherosclerosis. The purpose of this study is to investigate the potential antioxidant effect of dandelion polysaccharides in Wistar rats fed a high-fat diet. We find that dandelion polysaccharides reduce triglycerides, total cholesterol and low-density lipoprotein cholesterol and increase high-density lipoprotein cholesterol. cholesterol level. At the same time, dandelion polysaccharides reduce atherosclerotic lesions and increase collagen content. Dandelion polysaccharides increase the enzymatic activity of superoxide dismutase and glutathione peroxidase. As we know, Atherosclerosis is the accumulation of cholesterol plaques on the walls of the arteries, causing blockage of blood flow, which can occur as a result of a fatty diet. The choice of the Rota race is therefore relatively good, because it develops atherosclerosis in a relatively short time and that makes them an idol in research. Because atherosclerosis can remain asymptomatic for decades before clinical manifestations appear, even complex lesions can be clinically apparent, and some cases are not diagnosed until after death. Given the complexity and chronicity of atherosclerosis, animal models are relied upon to mimic human disease. Overall, these results suggest that dandelion polysaccharides play an important role in mitigating atherosclerosis through their antioxidant properties.

INTRODUCTION

The topic or research is based on the antioxidant properties of dandelion polysaccharides in atherosclerosis, because atherosclerosis is not only a serious chronic disease, but also the most common cause of death in many countries.

In India alone, the prevalence of coronary atherosclerosis is 78% in men and 66.6% in women.

Commission estimates that the absolute number of IHD patients in India will increase from 36 million in 2005 to 62 million in 2015 (a 70 percent increase).

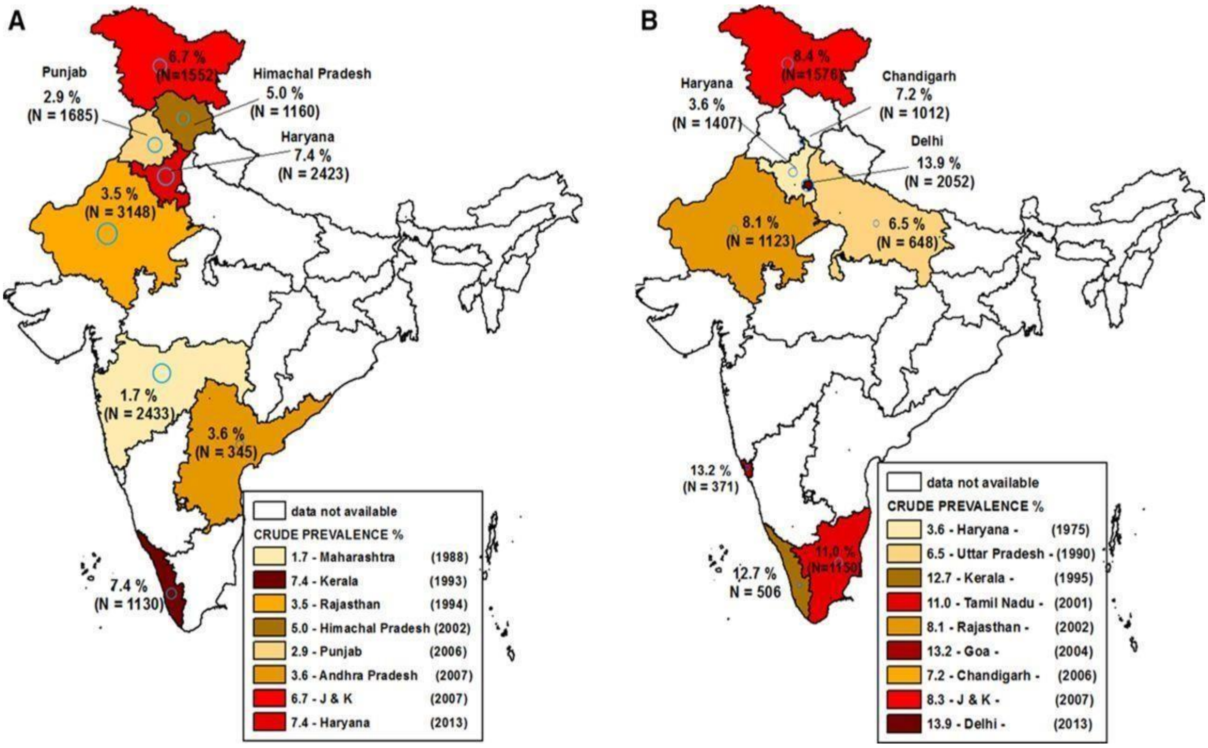

Figure 1

A. Prevalence of coronary heart disease in rural India. The numbers on the map are a breakdown; sample sizes are in parentheses. The years of the source data are given in parentheses in the index. Includes data from the new Haryana Rural Survey (2013) (D. Prabhakaran, unpublished data, 2013). B, Prevalence of coronary heart disease in urban India. Numbers on map are prevalence, sample sizes in parentheses. The years of the source data are given in parentheses in the index.

Although CVD risk factors are widespread in India, there are significant differences between and within different regions.

Social factors appear to play a particularly important role in determining outcomes after a CVD event. In the CREATE registry (the ACS Treatment and Outcomes Registry, which included 20,468 patients from 89 centers in 50 cities), outcomes after ACS were worse in patients with lower SES. For example, ACS-30-day mortality was 8.2% among the poor, 5.5% among the rich. This difference was largely due to differences in hospitalization and discharge medications. For example, a recent large cohort study in Mumbai showed that cardiovascular disease is no longer a disease of the rich. it affects the poor equally, with men of lower SES having higher CVD mortality. In case-control studies, low SES was associated with an increased likelihood of acute myocardial infarction. In the Jaipur Cross-sectional Study of Cardiovascular Risk Factors, suboptimal social characteristics such as low educational, occupational and SES status were associated with ≥ 3 cardiovascular risk factors and a higher Framingham risk score.

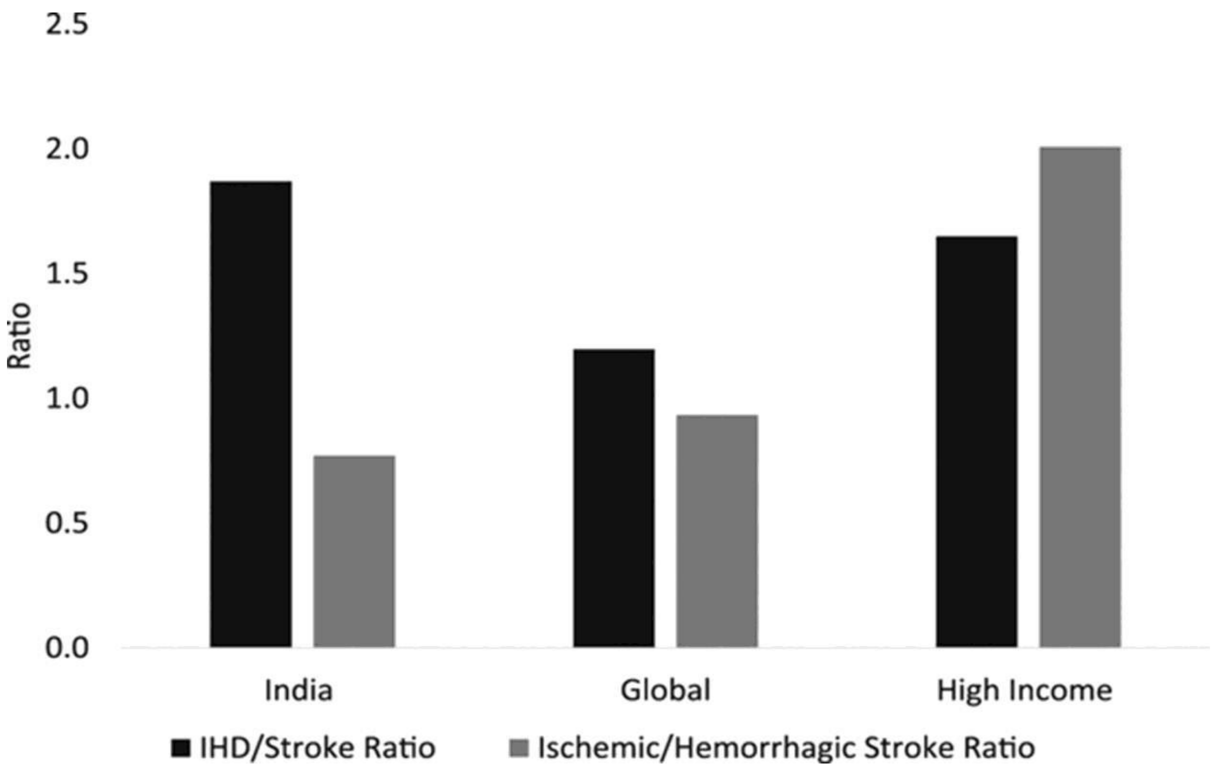

Figure 2

The ratio of ischemic heart disease to stroke and the ratio of ischemic to hemorrhagic stroke in India compared with global data. IHD is related to ischemic heart disease.

This makes the topic important to discuss, and compared to other herbs, dandelion is cheap and readily available. The polysaccharides in the dandelion plant make it ideal for atherosclerosis, which we believe lowers triglycerides, low-density lipoprotein cholesterol., total cholesterol levels and increases high-density lipoprotein cholesterol levels.

Figure 3 : Dandelion Plant (Taraxacum officinale)

The next topic deals with Wistar rats, because they develop atherosclerosis in a relatively short time, making them idols in research. They are kept on a high-fat diet for several days for research, and after a few days the screening process is carried out. .Rats have been widely used in physiological and metabolic studies. Besides the common advantage of small rodents, invasive procedures and sampling are easier to perform in rats compared to small mice.

Given the complexity and chronicity of atherosclerosis, animal models are relied upon to mimic human disease. Hyperlipidemia and hyperglycemia are associated with increased oxidative damage that affects antioxidant status and lipoprotein levels.

Studies have shown that lipid-lowering herbs can lower blood lipids, especially after meals, in addition to their antioxidant effects. Therefore, they can prevent atherosclerosis and vascular endothelial damage.

Overall, these results suggest that dandelion polysaccharides play an important role in mitigating atherosclerosis through their antioxidant properties.

There are a couple of valuable review papers addressing the pathogenesis of atherosclerosis.

The order in which the topic will be discussed are as follows:-

1. Atherosclerosis as a chronic & complex disease.

2. Scope & role of antioxidant in atherosclerosis.

3. Method of extraction of polysaccharide from the dandelion plant.

BODY:-

1. Atherosclerosis as a chronic and complex disease .

Atherosclerosis is a chronic inflammatory disease of large and medium-sized arteries that causes coronary heart disease, stroke, and peripheral vascular disease, collectively known as cardiovascular disease (CVD). It is a chronic inflammatory vascular disease involving the innate and adaptive immune system, which causes the formation of atheroma or plaques in the medium and large elastic or muscular arteries of the vascular wall, impairing arterial function.

Lesions occur at sites of endothelial damage, particularly overlapping fatty streaks and patchy intimal thickening. Intimate change, believed to be a physiological adaptation to mechanical stress, occurs in areas of the artery prone to atherosclerosis, such as branch points, branch ostia and arches.

Atherosclerosis is a complex disease resulting from a combination of genetic susceptibility, epigenetic changes and the interaction of environmental and systemic factors.

The atherosclerosis process:-

Fatty streaks formation. Atheroma formation.

Atherosclerotic plaques formation.

Fatty streaks both animal and human studies show that fatty streaks are the first sign of atherosclerosis. The initial damage is usually caused by the accumulation of lipoproteins in the inner lining of the arteries. One of the most important atherogenic lipoproteins is cholesterol-rich low-density lipoprotein (LDL). This lipoprotein can accumulate inside blood vessels due to its ability to penetrate the endothelium or attach to components of the extracellular matrix, such as proteoglycan. The relative increase in molecules of heparin sulfate compared to keratin sulfate and chondroitin sulfate can cause lipoprotein adhesion, which slows down intimate removal, which leads to their accelerated accumulation. [4,15]

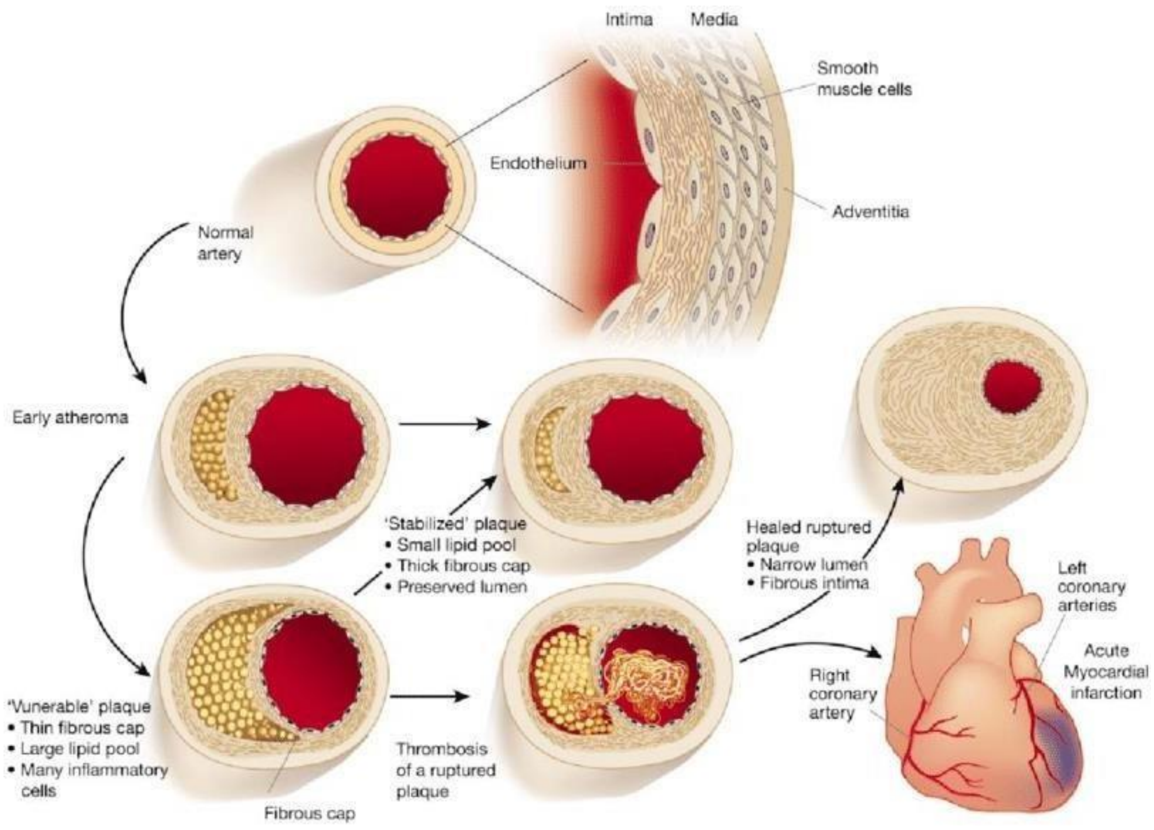

Figure 4: Atherosclerosis formation

In the early stages of atheroma formation, plaques usually grow in the opposite direction of the vessel. Atherosclerotic vessels tend to increase in diameter. If the plaque covers more than 40% of the inner elastic layer of the blood vessel, the ductus arteriosus is considered occupied. At the end of the plaque's life, a blockage restricts blood flow. Studies show that atherosclerosis is a consequence of intimal damage associated with a number of cellular responses involving monocytes, SMCs, and lymphocytes. During the process, the SMC multiply and in the final stages increase blood flow to the plaque.

Severe damage to vascular tissue occurs when adjacent SMC and endothelial cells secrete small peptides such as cytokines and growth factors such as interleukin 1 (IL-1) and TNF (which causes cells to grow). These factors cause SMC migration to the luminal side of the vessel wall. In this condition, smooth muscle cell migration and synthesized extracellular matrix form a fibrous cap. The fibrous cap is composed of collagen-rich fibrous tissue, SMC, macrophages, and T lymphocytes. They all form a mature atherosclerotic plaque and swell in the duct and reduce blood flow in the vessels.

Atherosclerotic plaque formation Atherosclerotic plaques constituents are as follows:

Vascular epithelium: The vascular epithelium reacts with macromolecules and blood components to increase the transfer of proteins in the plasma.[4]

Arterial smooth muscle: Maintenance of vascular repair and blood products, including lipid metabolism and secretion of various cytokines, is essential to control vascular wall tone.[4]

Lymphocytes: They can participate in immune reactions. The core of the plaque consists of cell damage, foam cells, calcium, cholesterol esters and a lot of fatty substances. The lipid core is a pale yellow mass, the color of which is caused by carotenoid pigments. [4,17,20]

Atherosclerosis risk factors.

The exact causes and risk factors of atherosclerosis are unknown; However, certain diseases, characteristics or habits can increase the chance of developing atherosclerosis. Most risk factors such as high cholesterol and LDL, low high density lipoprotein (HDL) blood levels, hypertension, cigarette smoking, diabetes, obesity, inactive lifestyle, age are controllable and atherosclerosis can be delayed or prevented.[13] 14,18]

As already discussed, the prevalence of atherosclerosis and subsequent mortality has already risen high, therefore, to prevent it, the extent and use of antioxidants in such a disease becomes important, because antioxidants can act through the following mechanisms: - \ n 1. Reactive oxygen concentration reduction.

2. Prevention of lipid chain oxidation by scavenging free radicals.

3. Suppression of the production of free radicals due to decomposition of peroxides of metal ion chelates.

4. Stopping the reaction chain to prevent the hydrogen absorption of the activated radical.[4,11,12,13,14,15,16]

Cholesterol is a hydrophilic lipid that is the stem cell of steroid hormones like this. like.

corticosteroids and sex hormones, bile acids and vitamin D. Cholesterol is an important part of the cell membrane. It has two sources, synthetic and dietary. Half of the body's cholesterol is obtained by synthesis, mainly in the liver of mammals, while all tissues containing nuclear cells are capable of synthesizing cholesterol.[21,22,23,24]

2. Scope and role of antioxidants in atherosclerosis.

Atherosclerosis begins with the formation of fatty streaks and progresses with the formation of atheroma and atherosclerotic plaque. Hypercholesterolemia, increase of LDL, decrease of HDL, oxidation of lipids, hypertension, insufficient production and dysfunction of NO, and inflammation are contributing factors to atherosclerosis, considering these issues, the role of antioxidants increases.

Many natural antioxidants have powerful antiviral effects. The effectiveness of flavonoids, i.e. (+)-catechin, luteolin, apigenin, quercetin and quercetin-7-rhamnoside, has been demonstrated against coronavirus infections (porcine epidemic diarrhea virus (PEDV), transmissible gastroenteritis virus (TGEV) [6,25, 26,27] \ n pro lack of effective treatments for diseases, antioxidants may prove to be an effective option to combat the SARS and MERS-CoV pandemic [32]. The place of action of antioxidants is the oxidative stress pathway, which plays a central role in the pathogenesis caused by the coronavirus. Diniz et al. [32] investigated the different effects of natural antioxidants against coronavirus, including reducing the protein expression of the nucleocapsid protein (N), 3C-like protease (3CLpro) [33,34,35,36] responsible for SARS-CoV. (quercetin and its derivatives) of reproduction.), papain-like protease (PLpro) (isovalcone and psoralidin)[37] and helicase protein due to efficient ATPase activity (myrcetin and scutellarein) [38].

A recently published review showed the benefit of antioxidants in the treatment of neurological disorders caused by COVID-19 [30]. However, reports that do not confirm the effectiveness of antioxidants in vivo cannot be ignored [31]. Antioxidant activity is mainly limited by ADMET (absorption, distribution, metabolism, excretion and toxicology) processes associated with poor absorption due to limitations in cell membrane penetration and degradation in the stomach and intestines. Low molecular weight antioxidants have also been reported to lose their ability to scavenge free radicals within cells. This is especially true for removal of hydroxyl radical (OH•), superoxide (O2•−) and H2O2 [28,29].

Small amounts of antioxidants can protect cell membranes and other body parts from oxidants. A balance between per- and antioxidants helps cells restore normal physiological function.

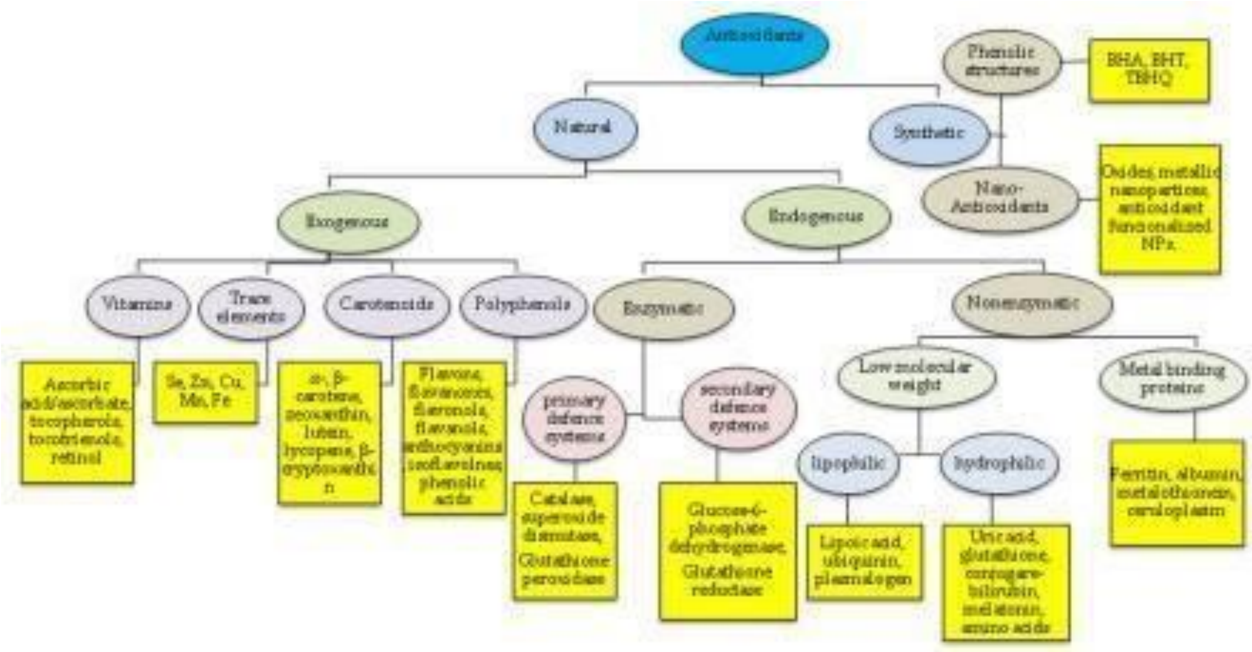

Figure 5: Classification of Antioxidants

In vitro peroxidation is influenced by the activity of enzymes such as superoxide dis- mutase, catalase and glutathione peroxidase. Ions such as Mn+2, Cu+2, Zn+2, Se+2 and Fe+2 act as antioxidant cofactors. Since lipid peroxidation is considered a key event in atherosclerosis, antioxidant protection is often associated with prevention of lipid peroxidation. Therefore, reducing the oxidative modification of lipoproteins in the body with natural and synthetic antioxidants is an effective way to prevent cardiovascular diseases. Rapid advances in the understanding of the molecular mechanisms of atherosclerosis have led to the discovery and proposals for mechanisms to delay the progression of coronary disease.

Dandelion polysaccharides are among herbs that contain antioxidants that fight atherosclerosis. As we already know, atherosclerosis causes narrowing of the arteries and restricts blood flow to the heart and other parts of the body, and antioxidants such as dandelion polysaccharides, which are rich in omega-3 fatty acids, can help prevent plaque build-up in the blood arteries Antioxidants reduced both cholesterol and radiation-induced circulating and tissue oxidized LDL, resulting in reduced plaque. Antioxidants can not only prevent the oxidation of triglycerides, but some of them can also prevent the oxidation of cholesterol.

Many naturally occurring antioxidants are now isolated, fully characterized and available for various applications as prophylactic and therapeutic agents to prevent the harmful effects caused by ROS.

Defense Mechanism of Antioxidants

An antioxidant is a molecule that can "neutralize" the oxidation of ROS before they react with cellular biomolecules and change their structure or function. Antioxidant protection has two levels[39,40]:

a. Primary defense mechanism: This defense mechanism prevents oxidative damage by directly trapping free radicals before they can damage intra- cellular biomolecules. Endogenous enzymes play an important role in this step [9,41,42]. The main defense mechanisms are summarized in the four stages shown below.

Superoxide dismutase (SOD) converts hydrogen peroxide (H2O2) to form superoxide radicals:

O−2+O−2+2H+−→−SODH2O2+O2

H2O2 is then converted by the enzymes catalase and glutathione peroxidase (GPx) to water and molecular to oxygen:

2H2O2−→−−−Catalase2H2O+O2

Glutathione peroxidase is an enzyme that catalyzes the reduction of H2O2 to water by glutathione (GSH):

H2O2+2GSH-→GPxGSSG+ 2H2H2 n

Glutathione disulfide (GSSG) is reduced back to GSH- by the action of reductase GSH-:

GSSG+NADPH+H+−→−−−−−−GSH reductase2GSH+NADP+

b. Vitamin C, vitamin E and uric acid scavenge free radicals as part of a secondary defense system. In addition, nuclear enzymes involved in DNA repair can be considered as a secondary defense system against oxidative damage caused by oxygen free radicals. Describes the protective effect of different antioxidants in the stage of atherosclerosis.

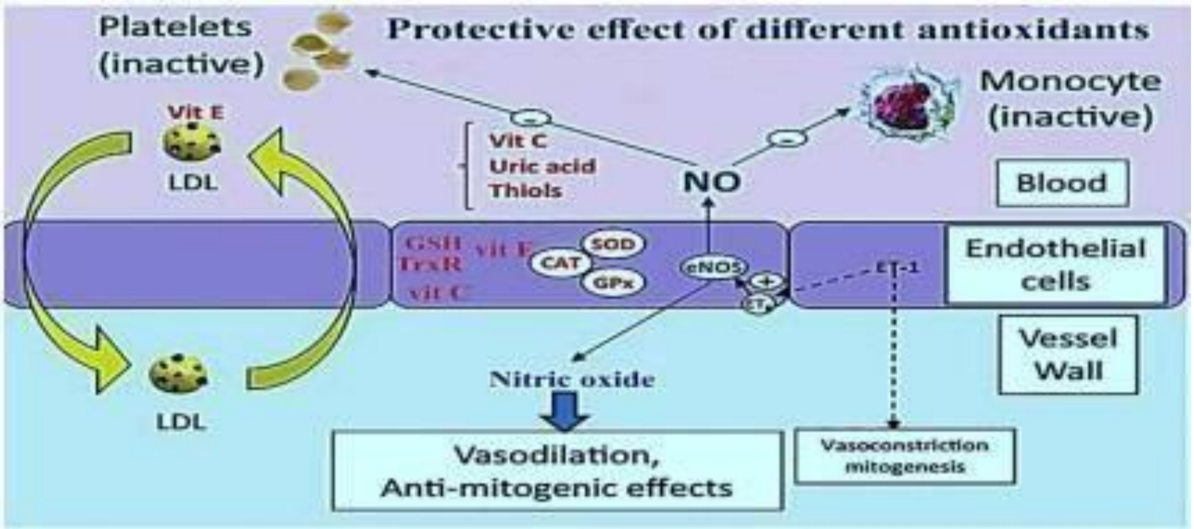

Figure 6: Mechanism of Antioxidants

In general, antioxidants can be divided into two groups: enzymatic and non-enzymatic antioxidants. Endogenous enzymatic antioxidants include superoxide dismutase (SOD), catalase (Cat), glutathione peroxidase (GPx), and thioredoxin reductase (TrxR).[41,42,43,44,45] Endogenous nonenzymatic antioxidants include glutathione. (GSH), uric acid, bilirubin, coenzyme Q (CoQ)/CoQH2) and lipoic acid [47].

As a result, dandelion polysaccharides can alleviate atherosclerosis and work better as an antioxidant.

3.Method of extraction of polysaccharide from the dandelion plant.

Polysaccharides have been associated with antioxidant activity using both in vitro chemical and biological models.

The antioxidant effect of polysaccharides largely depends on their solubility, sugar ring structure, molecular weight, presence of positively or negatively charged groups, protein parts and covalently linked phenolic compounds.

We found that polysaccharides significantly reduced serum triglycerides, total cholesterol, and low-density lipoprotein cholesterol, while increasing high-density lipoprotein cholesterol.

Polysaccharides, found in almost all organisms, are important functional biological macromolecules with significant health benefits.

They have antioxidant, antidiabetic, immune-strengthening, antitumor, anti- inflammatory and hypoglycemic effects.

And that is why it is effective in the treatment of atherosclerosis. These polysaccharides can be extracted by various methods.

As we are going to extract polysaccharides from the leaves of dandelion (Taraxacum) plant involving method using hot water extraction:

- Place the powdered dandelion leaves in the container.
- Add hot water (not boiling) to the container and stir well to form a suspension.
- Allow the mixture to steep for a certain period at a moderate temperature.
- After steeping, filter the mixture using cheesecloth or a fine sieve to separate the liquid extract from the solid residue.

All cells contain antioxidant systems that specifically scavenge superoxide or hydrogen peroxide or promote protection against ROS. Many antioxidant responses are regulated by Nrf2, an evolutionarily conserved transcription factor that is secreted under basal conditions but acutely upregulated during oxidant attack. Upon activation, Nrf2 dissociates from its repressor protein KEAP1, which reacts with oxidative radicals, translocate to the nucleus, binds to the antioxidant response element and induces the transcription of defense genes. As mentioned above, reduced expression and protein levels of Nrf2 and accompanying antioxidant protective activity are observed in tissues of COPD patients.

Enzymatic antioxidants convert oxidized metabolites to hydrogen peroxide and then to water in a multistep process using cofactors such as iron, zinc, copper and manganese. Hydrogen peroxide can also be converted to the powerful oxygen hypochlorous acid in the presence of chloride ions. This change is catalyzed by myeloperoxidase-extracted dandelion polysaccharides, which also act bidirectionally in the treatment of atherosclerosis with beneficial results as described above.

Cardiovascular disease (CVD) has been the leading cause of death for more than 20 years. The main causes are considered to be high cholesterol, obesity, smoking, diabetes and lack of exercise. One of the more commonly used treatment methods is a combination of anticoagulant and antithrombotic therapy; however, this often causes unwanted side effects. Therefore, the European Society of Cardiology recommends using a preventive strategy, including a varied diet rich in fruits, vegetables and herbs. All of them are sources of natural compounds with antiplatelet, anticoagulant or antioxidant properties, such as phenolic compounds. One such plant with multifaceted health-promoting effects and a rich source of secondary metabolites, including phenolic compounds, is dandelion (Taraxacum officinale).[67]

The most common forms of cardiovascular disease are atherosclerosis, high blood pressure, myocardial infarction, stroke and heart failure, and the main causes are high cholesterol, obesity, smoking, diabetes and lack of exercise. These symptoms are usually accompanied by changes in hemostasis.

One of the most common treatment strategies for cardiovascular disease is based on a combination of anticoagulant and antithrombotic therapy, including drugs such as aspirin, clopidogrel (thienopirin), rivaroxaban, warfarin, dabigatran and apixaban. These drugs act through several mechanisms [65,67]; for example, aspirin inhibits the production of thromboxane A2 (TXA2) by inhibiting cyclooxygenase activity in platelets, while clopidogrel blocks P2Y12 receptors on platelets. Unfortunately, the use of such drugs often results in unwanted side effects such as bleeding and ischemic complications in many patients.

The European Society of Cardiology recommends a varied diet rich in fruits, vegetables or herbs, which are sources of natural compounds with antiplatelet, anticoagulant or antioxidant effects. Dandelion (Taraxacum officinale) is also a good source of secondary metabolites such as phenolic compounds. A recent review detailed the chemical composition of dandelion, as well as its versatile antibacterial, anti- inflammatory, cytotoxic and diuretic properties.

However, the prophylactic and therapeutic potential of dandelion and its bioactive components against cardiovascular diseases and their effects on the cardiovascular system in general have not yet been discussed in any publication.

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