Annals of Science and Allied Research Vol. 3 (1) June, 2025: 48-60.
https://doi.org/10.5281/zenodo.15791134
ISSN – 2584-2307 (Online)

NATURAL VS. SYNTHETIC ANTIOXIDANTS: EFFICACY, SAFETY AND FUTURE TRENDS

Amanpreet Kaur[1]*, Neha Bhatt[2] , Shubhangee Agarwal[1], Priyanka Rani[1], Pawan Kumar Shukla[1], Sarika Arora[1] and Jugpal Singh[1]

[1, 1*]*Department of Chemistry, School of Sciences, IFTM University, Moradabad-244102, Uttarpradesh, India*
[2]*Department of Chemistry, Pt. L.M.S., Rishikesh Campus, SDS University, Tehri Garhwal- 249145, Uttarakhand, India*

(Received on April 08, 2025; Revised on June 7, 2025; Accepted on June 12, 2025)

ABSTRACT

Antioxidants are used to inhibit oxidation in foods, which causes rancidity and browning, as well as to prevent DNA damage, while also providing several beneficial physiological benefits in people. The concentration and absorption mechanism of natural antioxidants are crucial for achieving optimal therapeutic effects. The origins of antioxidants should be meticulously evaluated to optimize absorption and prevent the toxicity associated with elevated concentrations of synthetic compounds. A systematic initiative to inform consumers about foods abundant in natural antioxidants and to identify prominent synthetic antioxidants on food labels would be advantageous; nevertheless, more study is required to comprehensively comprehend their physiological impacts. Synthetic antioxidants are extensively used in the food industry to inhibit the oxidation of food matrices. They are used as dietary supplements for several health advantages, including cardiovascular disease prevention and anti-aging effects. Nonetheless, prolonged use of synthetic antioxidants has been associated with several ailments, including cancer. Concrete proof demonstrating their health risks is scarce. Additional research on the technical, health, and danger dimensions of synthetic antioxidants and their natural equivalents is necessary to enhance comprehension of these component categories.

Keywords: Natural antioxidants, oxidative stress, synthetic antioxidants, future possibilities

INTRODUCTION

The use of oxygen as the terminal electron acceptor in the oxidation of energy substrates derived from food enables aerobic organisms to generate substantial metabolic energy. The capacity of aerobic organisms to generate ATP is linked to the ongoing creation of radicals and other reactive oxygen species (ROS) that arise as byproducts of oxidative metabolism (1). The term antioxidant is defined, accompanied by an examination of the established categorization criteria: enzymatic and non-enzymatic, preventive or repair systems, endogenous and exogenous, primary and secondary, hydrosoluble and liposoluble, natural or synthetic (2). Primary antioxidants primarily function as chain terminators, capable of neutralizing radical species by hydrogen donation. Secondary antioxidants function as singlet oxygen quenchers, peroxide decomposers, metal chelators, oxidative enzyme inhibitors, or UV radiation absorbers (3). The precise method of action of the main representatives from each class of antioxidants (both endogenous and exogenous) in avoiding or mitigating certain variables that contribute to oxidative cellular damage (4). Mutual impacts, including synergistic effects, are examined and analyzed. Prooxidative impacts, such as those arising from the presence of transition metal ions, are also noted (5). Numerous studies have examined free radicals, oxidative stress, and the antioxidant activity of food, attributing a significant positive effect to antioxidants (6). However, newer writers have challenged their usefulness while seeking to elucidate the processes behind oxidative stress. Numerous experts assert that, irrespective of the amount of antioxidants consumed, absorption is significantly limited, and that in some instances, prooxidants may be advantageous to human health (7). The assessment of antioxidant activity and particular antioxidant chemicals may be conducted using many assays, each with distinct benefits and drawbacks (8,9). The debate regarding the in vivo benefits of antioxidants has intensified over the past few decades. This review aims to elucidate research on both natural and synthetic antioxidants, as well as prooxidants, highlighting their potential benefits and adverse effects, along with their mechanisms of action and detection methodologies. It also delineates the constraints of antioxidants and offers insights into prospective future developments in this domain (10).

Oxidative stress

Oxidative stress is characterized by an overproduction of reactive oxygen species that exceeds the neutralizing capacity of antioxidants, as well as a disruption of cellular redox equilibrium. Reactive oxygenated and nitrogenated species include superoxide anion radical, hydroxyl radical, alkoxyl radical, lipid peroxyl radical, nitric oxide, and peroxynitrite (11). This chapter examines the role of reactive oxygen species in causing oxidative damage to lipid membrane components, as well as the efficacy of antioxidants varying in structure, source, and mechanism of action—in combating oxidative stress (12). Oxidative stress induces structural alterations and functional modulation in nucleic acids, lipids, and proteins. Oxidative breakdown of lipids produces malondialdehyde, 4-hydroxynonenal, and isoprostanes from unsaturated fatty acids (13). Protein damage may arise via thiol oxidation, carbonylation, side-chain oxidation, fragmentation, unfolding, and misfolding, leading to a loss of function. 8-hydroxydeoxyguanosine serves as a biomarker for DNA damage (14). The role of reactive oxygenated and nitrogenated species in the manifestation of diseases is delineated. The imbalance between oxidant species and the antioxidant defense system may activate specific factors that contribute to oxidative cellular damage: overexpression of oncogenes, production of mutagenic compounds, enhancement of atherogenic activity, formation of senile plaques, or inflammation (15, 16). This results in cancer, neurodegeneration, cardiovascular disorders, diabetes, and renal problems. Different abiotic stressors result in the excessive generation of reactive oxygen species (ROS) in plants and animals, which are extremely reactive and toxic, causing damage to proteins, lipids, carbohydrates, and DNA, therefore inducing oxidative stress. Oxidative stress induces tissue damage and leads to several illnesses. Antioxidants counteract the effects of reactive oxygen species (ROS), hence aiding in disease prevention. Antioxidants may be either natural or synthetic. Natural antioxidants may be ingested via dietary sources, since they are found in fruits, vegetables, and spices (17). Certain synthetic antioxidants, such as BHT and BHA, also impede oxidation. Nonetheless, these synthetic antioxidants have been shown to pose risks to human health, prompting an expanded quest for non-toxic alternatives in recent years. Reactive oxygen species (ROS), often regarded only as detrimental agents in living organisms, have also been shown to fulfill beneficial functions (18, 19). This chapter elucidates ROS homeostasis, the ideas behind their examination, and the technological methodologies used to examine ROS-related activities. Particular emphasis is placed on challenges associated with the experimental recording of these processes, their variability, spatiotemporal distribution, and correlations with the physiological condition of the organisms (20). The disproportion between reactive oxygen species (ROS) production and removal, favoring the former, has been termed "oxidative stress," with specific implications for cellular physiology. Nearly 30 years have elapsed since Helmut Sies originally established the concept of oxidative stress; nonetheless, a recognized taxonomy of oxidative stress remains absent. A categorization of oxidative stress based on its severity is suggested to address this gap (21). Oxidative stress may be categorized into four classifications: baseline oxidative stress (BOS), low intensity oxidative stress (LOS), intermediate intensity oxidative stress (IOS), and high intensity oxidative stress (HOS) (22). A further categorization of possible relevance may distinguish three categories: mild oxidative stress (MOS), moderate oxidative stress (TOS), and severe oxidative stress (SOS) (23). Research directions in this domain encompass the advancement of intricate classifications of oxidative stress, precise identification of cellular reactive oxygen species (ROS) targets and their organized responses to ROS exposure, authentic in situ functions and mechanisms of purported "antioxidants," intracellular spatiotemporal distribution and effects of ROS, elucidation of molecular mechanisms governing cellular responses to ROS assaults, and the role of ROS in the execution of normal cellular functions within cellular homeostasis (24).

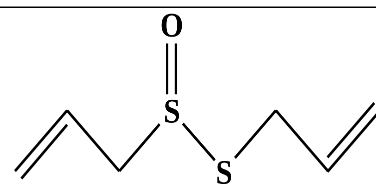
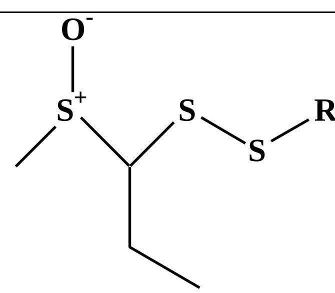
Natural antioxidants

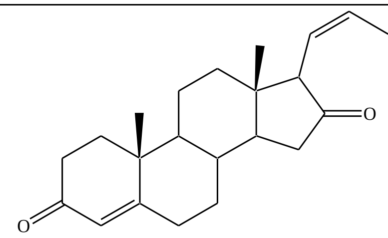
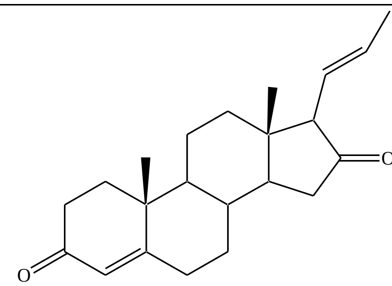
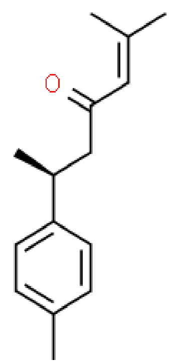
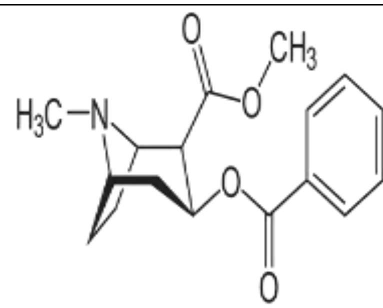
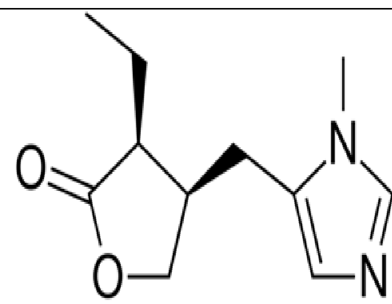
The interest in natural antioxidants arises from their widespread efficacy in diverse redox systems, leading to a wide range of potential applications: antioxidative phytochemicals are regarded as functional components in pharmaceuticals, functional foods, dietary supplements, animal feed, cosmetics, and other products (25). The interest in natural antioxidants for stabilizing lipid-containing meals has significantly grown due to

Annals of Science and Allied Research **Vol. 3 (1) June, 2025: 48-60.**
https://doi.org/10.5281/zenodo.15791134
ISSN – 2584-2307 (Online)

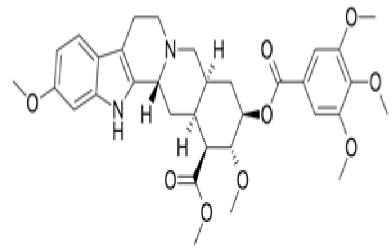
rising concerns over the potential toxicity of synthetic antioxidants and customer preferences for natural food additives. Plants are fundamental to life on Earth and an essential resource for humanity. All human consumption is directly or indirectly reliant on plants (26). Plants manage the hydrological cycle by spreading and purifying water via transpiration. They sequester carbon and control the concentrations of carbon dioxide and oxygen in the atmosphere. Plants further purify the air that humans inhale. Plants serve as a crucial source of pharmaceuticals. Since ancient times, plants have been traditionally used to treat several ailments and enhance human physical power (27). Medicinal plants are used globally, exhibiting little side effects and cost-effectiveness compared to other medical methods. Given the evolving circumstances, it is essential to augment and advocate for the protection and development of natural resources pertaining to medicinal plants (28). Alongside the need for conserving medicinal plants, it has also become imperative to safeguard and patent traditional and alternative medicines. Traditional medicinal systems based on botanical sources are widely used in many nations for various reasons (29, 30). The growth in population, adverse effects of many synthetic medications, insufficient drug supply, elevated treatment costs, and the emergence of resistance to existing antimicrobial agents have resulted in a heightened focus on the use of botanical resources. Diverse plant components, including as leaves, flowers, fruits, bark, and roots, are used to extract herbal medicines (31). Flowers and fruits are mostly employed in cosmetic items for personal care, while several essential oils, primarily derived from leaves, flowers, and fruits, are utilized in aromatherapy and other therapeutic applications (32). Consequently, given the aforementioned evidence, we deduce that plants constitute the essence of life on Earth today. Currently, research is on isolating physiologically active molecules from natural sources for illnesses where existing medications are not substantially successful. Herbal medicines are seeing a significant rebirth as an increasing number of individuals are shifting their focus from contemporary synthetic pharmaceuticals to ancient remedies, sometimes referred to as alternative medicine (33). Currently, several pharmaceuticals are directly extracted from medicinal plants and have been used without any structural alterations by various pharmaceutical companies (34). In recent years, several new chemicals have been extracted from plants, and many of these molecules have shown noteworthy biological functions. Secondary metabolites have been important in medication discovery.

Table 1 Use and structure of drugs derived from medicinal plants

Plant name	Drug	Used in ailment	Structure
Allium sativum	Alliin	Cardioprotective, antidiabetic	
Allium caepa	Cepaene	Reducing cholesterol	

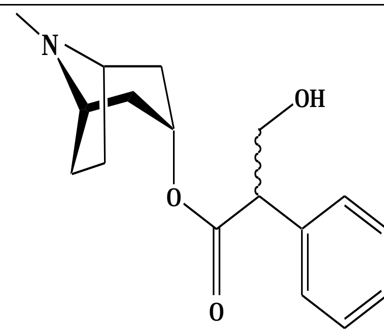
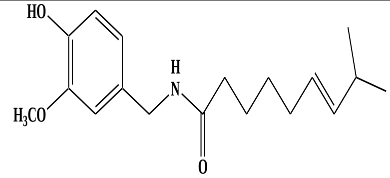
Commiphora mukul	Z-guggulsterne	*Antiplatelet*, improving thyroid	
	E-guggulsterne	Reduce cholesterol, improving the liver ability	
Curcuma longa	turmerone	Antifungal, Anti-inflammatory, antidermatophytic	
Erythroxylum coca	Cocaine	Local anesthetics, cerebral stimulant (Narcotic use)	
Pilocarpus jaborandi	Pilocarpine	Treatment of glaucoma	

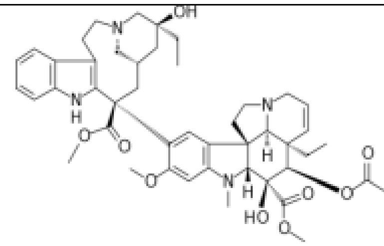
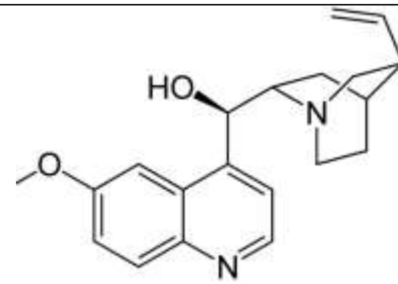
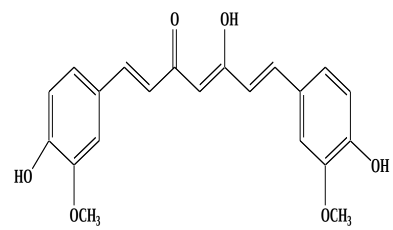
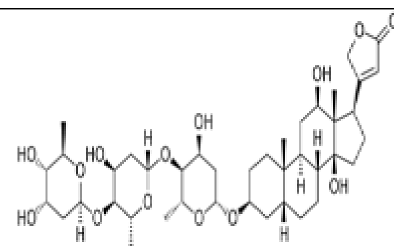
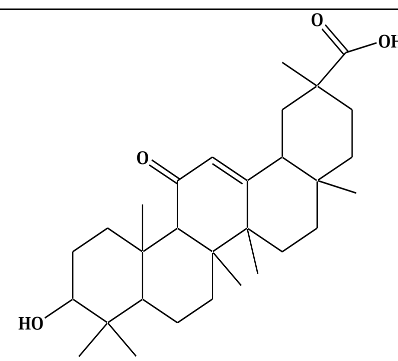
Annals of Science and Allied Research Vol. 3 (1) June, 2025: 48-60.
https://doi.org/10.5281/zenodo.15791134
ISSN – 2584-2307 (Online)

Rauwolfia serpentina	Reserpine	Antihypertensive, tranquilizer	

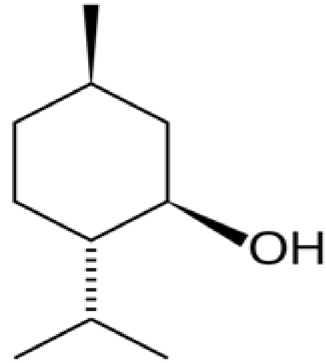
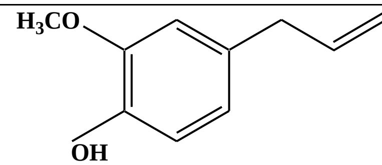
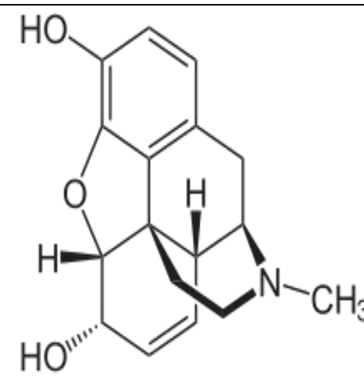
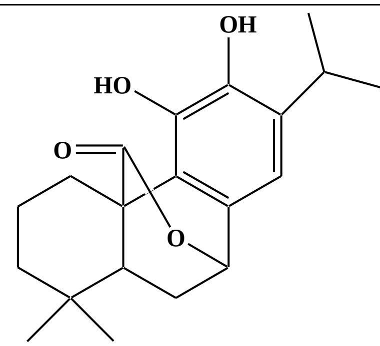
Phenolic and polyphenolic substances have a significant function as natural antioxidants (35). Phenolic chemicals, prevalent in plants, are a vital component of the human diet and are of significant interest owing to their antioxidant characteristics and possible health benefits (36). These compounds exhibit a structural spectrum from basic phenolic molecules to intricate high-molecular-weight polymers (37). Growing data suggests that the intake of certain phenolic compounds found in foods may reduce the incidence of health issues due to their antioxidant properties (38). Antioxidants, when included into foods, inhibit rancidity, impede the generation of harmful oxidation byproducts, preserve nutritional integrity, and prolong product shelf-life (39). In light of safety concerns and restrictions on synthetic antioxidants, there is growing interest in natural antioxidants derived from consumable materials, by-products, and residual sources. This work delineates both synthetic and natural phenolic antioxidants, highlighting their mechanisms of action, health implications, degradation products, and toxicological profiles. The table below lists some phenolic natural antioxidant compounds.

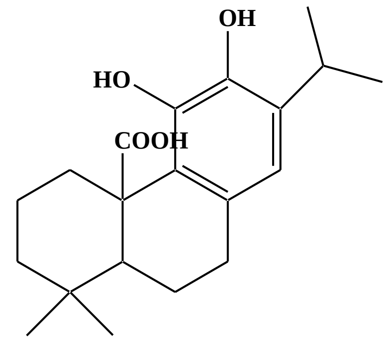
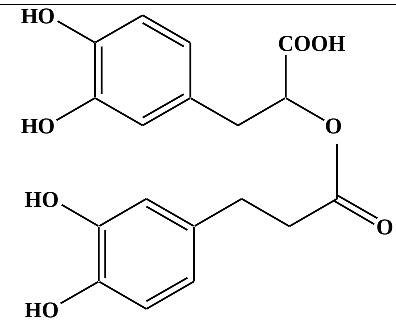
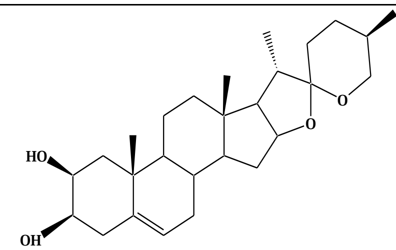
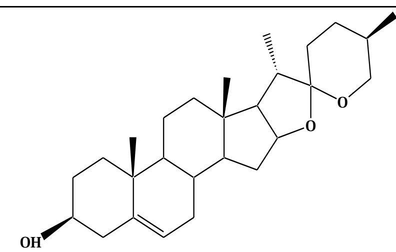
Table 2 Phenolic compounds as a natural antioxidant

Plant name	Drug	Used in ailment	Structure
Atropa belladonna	Atropine	Mydriatic, anhydrotic, anti spasmodic	
Capsicum annuum	Capsaicin		

Catharanthus roseus	Vinblastine	Hodgkin's lymphoma, choriocarcinoma	
Cinchona officinalis	Quinine	Analgesic, antipyretic, antimalarial	
	Curcumin	Antianxiety, antioxidant, treatment of obesity	
Digitalis lanata	Digoxin	Cardiotonic	
Glycyrrhiza glabra	Glycyrrhetica acid	Anti- inflammatory, peptic ulcer treatment	

Annals of Science and Allied Research Vol. 3 (1) June, 2025: 48-60.
https://doi.org/10.5281/zenodo.15791134
ISSN – 2584-2307 (Online)

Mentha arvensis ***Mentha piperita***	Menthol	Local anaesthetic, counterirritant, Antipruritic, counterirritnt, stimulant	
Ocimum sanctum	Eugenol	Reduction in total cholesterol, antioxidant	
Papver somniferum	Morphine	Narcotic analgesic	
Rosemarinus officinalis	Carnosol	Antioxidant, antidiabetic, anticancerous	

	Carnosinic acid	Antioxidant, antidiabetic, neuroprotective	
	Rosmarinic acid	Antioxidant, antipertensive effect	
Trigonella foenum graecum	Diosgenin	Reduce cholesterol, antioxidant	
	Gitogenin	Antioxidant	

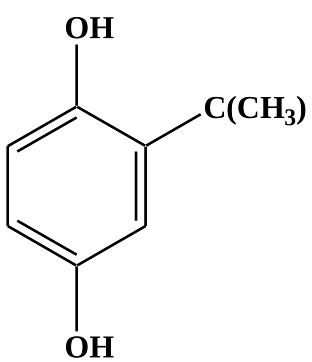
Synthetic antioxidants

Synthetic antioxidants are artificially produced chemicals that do not exist in nature and are included into food as preservatives to inhibit lipid oxidation (40, 41). Synthetic antioxidants, in contrast to natural ones, are extensively used in the food business because to their varied raw material sources, established technology, cost-effectiveness, minimal side effects, effective scavenging action, and simplicity of acquisition (42, 43). Owing to the intrinsic volatility of natural antioxidants, several synthetic antioxidants have been used to stabilize fats and oils. Currently, the predominant synthetic antioxidants utilized in food are phenolic antioxidants, such as butylated hydroxyanisole (BHA, E-number 320), butylated hydroxytoluene (BHT, E-number 321), tertiary butylhydroquinone (TBHQ, E-number 319), and propyl gallate (PG, E-number 310), which serve to preserve dietary fats and oils. Butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) were first formulated to safeguard petroleum from oxidative gumming (44, 45). These chemicals have served as antioxidants in human food since 1954 and are perhaps the most prevalent antioxidants used in such meals today. BHT and BHA possess similar nomenclature, structural characteristics, and antioxidant efficacy, and are often used in conjunction within fats and oils.

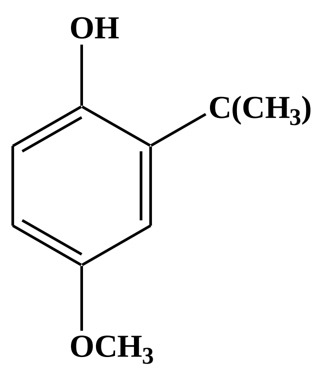
Annals of Science and Allied Research **Vol. 3 (1) June, 2025: 48-60.**
https://doi.org/10.5281/zenodo.15791134
ISSN – 2584-2307 (Online)

Although both BHT and BHA are classified as "generally recognized as safe" chemicals (46). Some chronic toxicity investigations have identified BHT as a possible tumor promoter when administered at elevated doses. Conversely, BHA and BHT may serve as significant inhibitors of carcinogenesis, likely via their antioxidant properties. Consequently, efforts have been made to eliminate these antioxidants; TBHQ (tert-butylhydroxyquinone) is a prevalent synthetic antioxidant used in the feed business. Similar to BHT and BHA, TBHQ has a benzene ring or phenolic structure (47). Additional instances of synthetic antioxidants include propyl gallate (PG), dodecyl gallate (DG), octyl gallate (OG), and ethylene diaminetetraacetic acid (EDTA) (48). Synthetic phenolic antioxidants (SPAs) may interact with peroxides produced in food under certain circumstances to inhibit the degradation process, so significantly enhancing food stability and prolonging shelf life (49). Consequently, the appropriate use of antioxidants may provide significant economic advantages for producers while simultaneously ensuring safer food for consumers (50). The toxicity of BHA, BHT, and TBHQ has been thoroughly examined under many experimental settings. Research indicates that the acute toxicity of BHA is minimal, with a lethal dosage 50 (LD50) value in mice and rats exceeding 2000 mg/kg body weight. Studies indicate that BHA has a significant cytotoxic impact on human astrocytes (51, 52) and developmental toxicity in zebrafish embryos/larvae (53). The results of the zebrafish embryo toxicity test (ZFET) indicated that BHT exhibited cardiotoxicity and may serve as a possible teratogen for aquatic creatures (54). The in vivo investigation indicated that PG may promote testicular toxicity by impairing mitochondrial or endoplasmic reticulum function and suppressing genes associated with testicular development (55).

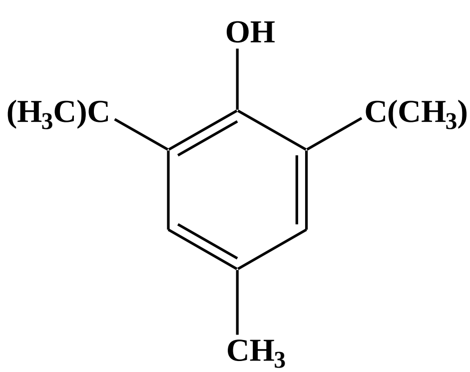
Structure of some synthetic antioxidants



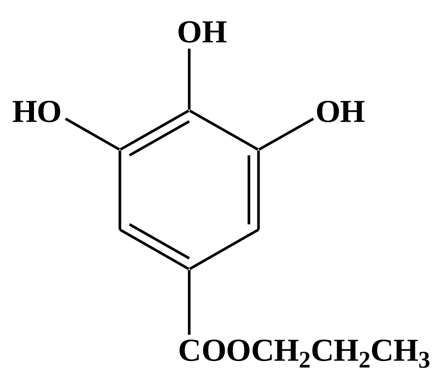
Tertiary butylhydroquinone (TBHQ)



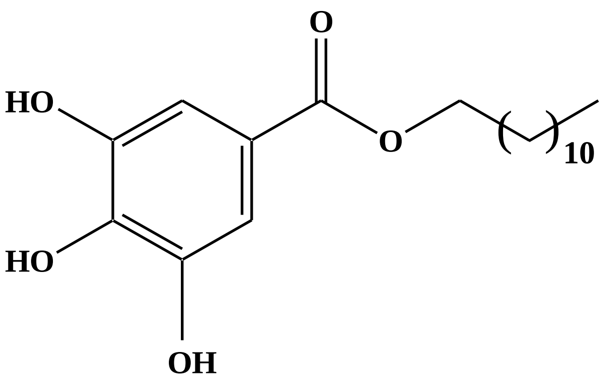
Butylated hydroxyanisole (BHA)



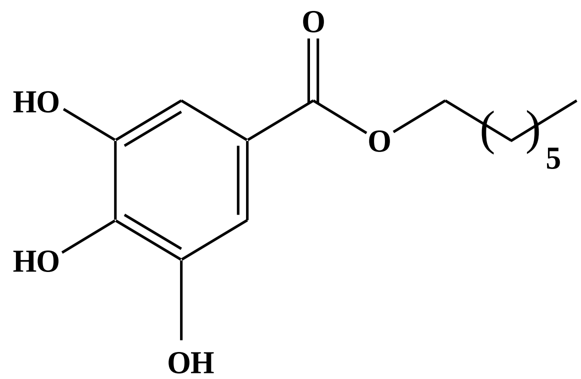
Butylated hydroxytoluene (BHT)



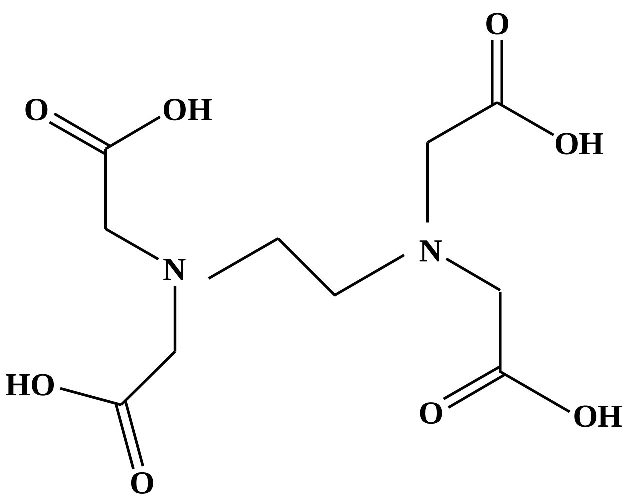
Propyl gallate



Dodecyl gallate



Octylgallate



Ethylene diaminetetraacetic acid

Future consideration

Antioxidants are a crucial element of the ROS-dependent signaling network and serve as a defense against the overproduction of ROS. Recent investigations raise questions about the advantages of prolonged antioxidant supplementation, partially due to the organism's propensity to maintain redox equilibrium; yet, the detrimental consequences of antioxidant shortage are evident (56). Numerous instances demonstrate the effective use of antioxidants to mitigate the pathological consequences of oxidative stress. Innovative methods for antioxidant administration, such as the incorporation of nanoparticles, have been suggested, and novel antioxidants especially aimed at mitochondria, the primary biological generator of reactive oxygen species (ROS), have been produced and are undergoing testing. An alternative method may include the activation of gene expression for antioxidant proteins or the implementation of antioxidant gene therapy (57). Meticulous examinations of their effectiveness and adverse effects are requisite. The widespread preference for naturally derived chemicals is significant and drives the quest for more effective antioxidants in nature. Considering that oxidative stress is contingent upon both the production of reactive oxygen species (ROS) and their elimination by antioxidants, inhibitors of ROS-generating enzymes are also evaluated and may have potential applications for mitigating the effects of oxidative stress; such compounds may also be regarded as antioxidants in a broader biomedical context. Given these factors, it is reasonable to anticipate that antioxidant research will continue to be very busy in the next years (58). Growing data suggests that the intake of various phenolic compounds found in natural foods may reduce the incidence of severe health conditions due to their antioxidant properties, among other processes. The mechanisms of action of various phenolic compounds in certain organs must be elucidated. Given the safety and various constraints associated with synthetic antioxidants, natural antioxidants derived from consumable sources, by-products, and co-products provide alternate sources of interest (59). Additional research on the extraction of phenolic compounds by complementary techniques and their impact on antioxidant levels in animal models and human participants is necessary to assess their potential advantages. Furthermore, it is essential to validate the absence of toxicity and the bioavailability of the natural phenolic extract. The provision of isolated phenolics as dietary supplements or functional food components for health enhancement and illness risk mitigation may further enhance the effectiveness of these substances (60).

In foods susceptible to oxidation, antioxidants serve as inhibitors of oxidation events via many ways. However, several foods lack natural antioxidants and are prone to degradation during processing or storage, requiring the use of synthetic antioxidants. Nevertheless, the majority of synthetic antioxidants exhibit efficacy at modest doses, whereas the incorporation of elevated quantities may induce a pro-oxidant impact (61). Moreover, substantial quantities of synthetic antioxidants have been shown to pose safety concerns. Consequently, prudence is essential while choosing and incorporating antioxidants into dietary systems. Simultaneously, the safety of natural antioxidants should not be overlooked, since those derived from natural sources are garnering increasing attention. To get a diverse array of antioxidants in the diet, one should consume foods that include all hues of the rainbow (62). Each hue has distinct antioxidant properties. Vivid orange and rich yellow fruits and vegetables, such as carrots, sweet potatoes, and apricots, provide a specific category of antioxidants. Red foods, such as tomatoes, provide an additional benefit. Green veggies, like broccoli and cabbage, together with blue or purple foods, such as blueberries, possess distinct antioxidant profiles.

Conclusion

Antioxidants, whether derived from natural or synthetic sources, are essential in alleviating oxidative stress, therefore improving general health and perhaps prolonging lifetime. A healthy diet should include natural antioxidants derived from plants, fruits, vegetables, and herbs, owing to their superior absorption, negligible side effects, and synergistic benefits. Synthetic antioxidants exhibit effectiveness and cost-effectiveness; yet, apprehensions about their safety, toxicity, and long-term health consequences remain. Natural compounds, in contrast to synthetic antioxidants, have superior safety and environmental compatibility; yet, they exhibit diminished stability and efficacy. Innovative extraction techniques, structural modifications, and breakthroughs in nanotechnology may improve their therapeutic effectiveness. Antioxidants are used in medications, food preservation, cosmetic formulations, and biological research techniques. Scientific advancements suggest that incorporating antioxidants into innovative formulations and delivery systems is anticipated to improve their effectiveness and expand their uses. A holistic strategy that integrates both natural and synthetic antioxidants will be crucial in the future. Continuous research is essential for improving the stability, efficacy, and safety of natural antioxidants, as well as for creating safer synthetic replacements. The extraction and production of sustainable antioxidants will aid in environmental conservation initiatives. Antioxidant research has considerable promise for improving human health and mitigating oxidative damage. An interdisciplinary strategy that amalgamates chemistry, biology, pharmacology, and technology is vital to augment their application.

REFERENCES

1. Abbas, MN., Pomegranate peels: Source of antioxidants extraction and natural dentifrices preparation, *Europ Acad Res*, **2014**, 2, 3078–3089.
2. Chen, AY.; Chen, YC., A review of the dietary flavonoid, kaempferol on human health and cancer chemoprevention, *Food Chem,* **2013**, 138, 2099-2105.
3. Aslam, MS.; Ahmad, MS., Worldwide Importance of Medicinal Plants: Current and Historical Perspectives, *Rec Adv Biol Med.* **2016**, 2, 88-93.
4. Augustyniak, A.; Bartosz, G.; CˇIpak, A.; Duburs, G.; Horáková, L.; Uczaj, W.; Majekova, M.; Odysseos, AD.; Rackova, L.; Skrzydlewska, EZB.; Stefek, M.; Trosová, M.; Tirzitis, G.; Venskutonis, PR.; Viskupicova, J.; Vraka, PS.; Arkovic, N., Natural and synthetic antioxidants: An updated overview. *Free Rad Res.,* **2010,** 44, 1216–1262.
5. Barbalace, MC.; Zallocco, L.; Beghelli, D.; Ronci, M.; Scortichini, S.; Digiacomo, M.; Macchia, M.; Mazzoni, MR.; Fiorini, D.; Lucacchini, A.; Ronci, M.; Hrelia, S.; Giusti, L.; Angeloni, C., Antioxidant and Neuroprotective Activity of Extra Virgin Olive Oil Extracts Obtained from Quercetano Cultivar Trees Grown in Different Areas of the Tuscany Region (Italy). *Antioxidants*, **2021**, 10, 421.
6. Basu, A.; Betts, NM.; Mulugeta, A.; Tong, C.; Newman, E.; Lyons, TJ.; Green tea supplementation increases glutathione and plasma antioxidant capacity in adults with the metabolic syndrome. *Nutri Res*, **2013**, 3, 180-187.
7. Carocho, M.; Ferreira, ICFR., A review on antioxidants, prooxidants and related controversy: Natural and synthetic compounds, screening and analysis

methodologies and future perspectives, *Food Chem Toxic,* **2013**, 51, 15–25.

8. Cosme, P.; Rodríguez, AB.; Espino, J.; Garrido, M., Plant Phenolics: Bioavailability as a Key Determinant of Their Potential Health-Promoting Applications, *Antiox.* **2020**, 9, 1263.
9. Daiber, A.; Kröller-Schön, S.; Frenis, K.; Oelze, M.; Kalinovic, S.; Vujacic-Mirski, K.; Kuntic, M.; Bayo Jimenez MT.; Helmstädter, J.; Steven, S.; Korac, B.; Münzel, T., Environmental noise induces the release of stress hormones and inflammatory signaling molecules leading to oxidative stress and vascular dysfunction-Signatures of the internal exposome. *Biofactors*. **2019** 45, 495-506.
10. Danta, CC.; Piplani, P., The discovery and development of new potential antioxidant agents for the treatment of neurodegenerative diseases. *Expert Opin. Drug Discov.* **2014**, 9(10), 1-18.
11. Donato, A.J.; Machin, D.R.; Lesniewski, L.A., Mechanisms of Dysfunction in the Aging Vasculature and Role in Age-Related Disease. *Circ. Res.* **2018**, 123, 825–848.
12. Feresin, RG.; Johnson, SA.; Pourafshar, S.; Campbell, JC.; Jaime, SJ.; Navaei, N; Elam, ML.; Akhavan, NS.; Alvarez-Alvarado, S.; Tenenbaum, G.; Brummel-Smith, K.; Salazar, G.; Figueroa, A.; Arjmandi, BH., Impact of daily strawberry consumption on blood pressure and arterial stiffness in pre- and stage 1-hypertensive postmenopausal women: A randomized controlled trial. *Food Funct.,* **2017**, 8, 4139–4149.
13. Flack, JM.; Adekola, B., Blood pressure and the new ACC/AHA hypertension guidelines. *Trends Cardiovasc. Med.,* **2020**, 30, 160–164.
14. Gangola, S.; Khati, P.; Bhatt, P.; Sharma, A., India as the Heritage of Medicinal Plant and their Use. *Curr Trends Biomedical Eng Biosci*., **2017**, 4(4), 1-2.
15. Ham, J.; Lim, W.; You, S.; Song, G., Butylated hydroxyanisole induces testicular dysfunction in mouse testis cells by dysregulating calcium homeostasis and stimulating endoplasmic reticulum stress, *Science of the Total Environment,* **2020**, 702:134775.
16. Ham, J.; Lim W.; Park S.; Bae H.; You S.; Song G., Synthetic phenolic antioxidant propyl gallate induces male infertility through disruption of calcium homeostasis and mitochondrial function, *Environ Pollu,* **2019**, 248, 845–856, https://doi.org/10.1016/j.envpol.2019.02.087.
17. Hano C.; Abbasi BH., Plant-Based Green Synthesis of Nanoparticles: Production, Characterization and Applications, *Biomole,* **2022**, 12, 1-9.
18. Hassan FU.; Rehman MSU.; Khan MS.; Ali MA.; Javed A.; Nawaz A.; Yang C., Curcumin as an Alternative Epigenetic Modulator: Mechanism of Action and Potential Effects. *Front. Genet*., **2019**, 10, 514.
19. Hrelia S.; Angeloni C., New Mechanisms of Action of Natural Antioxidants in Health and Disease II, *Antioxidants*, **2021**, 10, 1-6.
20. Jeremi´c S.; Radenkovi´c S.; Filipovi´c M.; Anti´c M., Ami´c A.; Markovi´c Z., Importance of hydrogen bonding and aromaticity indices in QSAR modeling of the antioxidative capacity of selected (poly)phenolic antioxidants, *J Mole Graph Model,* **2017**, 72, 240–245.
21. Johnson SA.; Feresin RG.; Navaei N.; Figueroa A.; Elam ML.; Akhavan NS.; Hooshmand S.; Pourafshar S.; Payton ME.; Arjmandi BH., Effects of daily blueberry consumption on circulating biomarkers of oxidative stress, inflammation, and antioxidant defense in postmenopausal women with pre- and stage 1-hypertension: A randomized controlled trial, *Food Funct*, **2017**, 8, 372-380.
22. Kaur A.; Shukla A.; Shukla RK., Comparative Evaluation Of ABTS, DPPH, FRAP, Nitric Oxide Assays For Antioxidant Potential, Phenolic & Flavonoid Content Of Ehretia acuminata R. Br. Bark, *Int Res Journal Pharm,* **2018**, 9(12), 100-104.
23. Keenan, T.D., Agrón, E., Keane, P.A., Domalpally, A., Chew, E.Y., Study, A.R.E.D., Group, R. and Age-Related Eye Disease Study Research Group. Oral antioxidant and lutein/zeaxanthin supplements slow geographic atrophy progression to the fovea in age-related macular degeneration. *Ophthalmology*, **2025**, *132*(1), 14-29.
24. Kaur A.; Shukla A.; Shukla RK., In vitro antidiabetic and anti-inflammatory activities of Ehretia acuminata R. Br. bark, *Ind J Nat Prod Res*., **2021**, 12(4), 538-543.
25. Kumar J., An ayurvedic perspective on food safety. Chapter 6 - An ayurvedic perspective on food safety, *Food Safety in the 21st Century Public Health Perspective*, **2017**, 71-81.
26. Krzemi´nska J, Wronka M, Młynarska E, Franczyk B, Rysz J. Arterial Hypertension-Oxidative Stress and Inflammation. Antiox 2022;11:1-20.
27. Lorenzo DC.; Colombo F.; Biella S.; Stockley C.; Restani P., Polyphenols and Human Health: The Role of Bioavailability, *Nutrients*, **2021**, 13, 273.
28. İzol E, Turhan M, Yılmaz MA, Çağlayan C, Gülçin İ. Determination of Antioxidant, Antidiabetic, Anticholinergic, Antiglaucoma Properties and Comprehensive Phytochemical Content by LC-MS/MS of Bingöl Honeybee Pollen. Food Science & Nutrition. **2025**, 13(3):4531.
29. Liang L.; Wu X.; Zhao T.; Zhao J.; Li F.; Zou Y.; Mao G.; Yang L., In vitro bioaccessibility and antioxidant activity of anthocyanins from mulberry (Morus atropurpurea Roxb.) following simulated gastro-intestinal digestion. *Food Res. Int.* **2012**, 46, 76–82.
30. Park S.; Lee JY.; Lim W.; You S.; Song G., Butylated hydroxyanisole exerts neurotoxic effects by promoting cytosolic calcium accumulation and endoplasmic reticulum stress in astrocytes, *Journal of Agricultural and Food Chem.* **2019**, 67(34), 9615–9629.
31. Aouadi A., Saoud DH., Laouini SE., Rebiai A., Achouri A., Mohammed HA., Bouafia A., Abdullah JA., Alharthi F. Synergistic chitin-zinc nanocomposites from shrimp shell waste: characterization, antioxidant, and antibacterial properties. Biomass Conversion and Biorefinery. **2025**, 15(1):545-61.
32. Raja K.; Balamurugan V.; Selvakumar S.; Vasanth K., Striga Angustifolia Mediated Synthesis of Silver Nanoparticles: Anti-microbial, Antioxidant and Anti-proliferative Activity in Apoptotic P53 Signalling Pathway, *J. Drug Deliv. Sci. Technology*, **2022**, 67, 102945. Doi:10.1016/J.JDDST. 2021.102945.

33. Halliwell, B. Understanding mechanisms of antioxidant action in health and disease. *Nature Reviews Molecular Cell Biology*, **2024**, *25*(1),13-33.
34. Rao RV., Ayurveda and the science of aging, *J Ayurveda Integr Med*, **2018**, 9, 225-232.
35. Said M. Al-Dalaen; Aiman I. Al-Qtaitat, Review article: Oxidative stress versus antioxidants, *Amer J Biosci Bioeng*, **2014**, 2(5), 60-71.
36. Sarkar M., Devi A., Analysis of medicinal and economically important plant species of Hollongapar Gibbon wildlife sanctuary, Assam, northeast India, *Trop plant res.* **2017**, 4(3), 486–495.
37. Silvestrini, A., Meucci, E., Ricerca, B.M. and Mancini, A. Total antioxidant capacity: biochemical aspects and clinical significance. *International journal of molecular sciences*, **2023**, *24*(13), p.10978.
38. Sarmah R.; Kanta BS.; Dutta R.; Nath D.; Pokhrel H.; Mudoi LP.; Sarmah N.; Sarma J; Ahmed AM.; Nath RJ.; Ingtipi L., Toxicity of a synthetic phenolic antioxidant, butyl hydroxytoluene (BHT), in vertebrate model zebrafish embryo (Danio rerio), *Aqua Res.* **2020**, 51(9), 3839–3846.
39. Shahidi F.; Ambigaipalan P., Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects: A review, *J func foods*, **2015**, 1-78.
40. Shukla A.; Anchal.; Shukla RK.; Kaur A., Isolation and Identification of two triterpenoids from ethyl acetate extract of bark of Boehmeria rugulosa, *Research Journal of Pharmacy and Technology*, **2021**, 14(6), 2919-2923.
41. Shukla A.; Kaur A., A Systematic Review Of Traditional Uses Bioactive Phytoconstituents Of Genus Ehretia, *Asian J Pharm Clinical Res.*, **2018**, 11(6), 88-100.
42. Shukla A.; Kaur A.; Shukla RK.; Anchal. A., Comparative Study of In Vitro Antioxidant Potential, Photoprotective Screening of Ehretia acuminata R.*Br.* Leaves, *Indian Drugs*. **2019**, 56(9), 30-36.
43. Shukla A.; Kaur A.; Shukla RK.; Anchal., Comparative Evaluation of Antioxidant capacity, Total flavonoid and Phenolic content of Ehretia acuminata R. Br. fruit. *Res J Pharm Tech*, **2019,** 12(4), 1811-1816.
44. Shukla A.; Kaur A.; Shukla RK., Evaluation of different biological activities of leaves of Ehretia acuminata R.B*r*, *Ind Drugs*, **2021**, 58(4), 42-49.
45. Shukla RK.; Nandan K.; Shukla A.; Kaur A., Nutritional importance and phytochemical investigation of sepals of Bombax ceiba Linn, *Plant archives.* **2020**, 20, 100-103.
46. Shukla RK.; Nandan K.; Shukla A.; Kaur A.; Phytochemical analysis and nutritive value of Bombax ceiba Linn. Plant archives. **2020,** 20, 1201-1206.
47. Shukla RK.; Nandan K.; Shukla A.; Kaur A.; Rana D., Review on Traditional uses, Biological activities, Phytoconstituents of Bombax ceiba Linn. *Res J Pharm Tech.* **2020**, 13(11), 5607-5612.
48. Shukla A.; Pokhriyal P.; Shukla RK.; Kaur A., A green and facile approach for antidiabetic and anti-inflammatory potency for Fiscus subincisa fruit. *Indian drugs*, **2021**., 58(8), 68-74.
49. Sindhi V.; Gupta V.; Sharma K.; Bhatnagar S.; Kumari R.; Dhaka N., Potential applications of antioxidants e A review, *J pharm res* **2013**, 7, 828-835.
50. Sun Y.; Lu Y.; Saredy J.; Wang X.; Drummer IC.; Shao Y.; Saaoud F.; Xu K.; Liu M.; Yang WY.; Jiang X., ROS systems are a new integrated network for sensing homeostasis and alarming stresses in organelle metabolic processes, *Redox Biol.*, **2020,** 37, 101696.
51. Taravati A.; Tohidi F., Comprehensive analysis of oxidative stress markers and antioxidants status in preeclampsia, *Taiwan J. Obstet. Gynecol.* **2018**, 57, 779–790.
52. Thalluri J., A research on medicinal plants, *Res Rev: J Med Org Chem.*, **2016**, 3(2), 157-165.
53. Touyz RM.; Rios FJ.; Alves-Lopes R.; Neves KB.; Camargo LL.; Montezano AC., Oxidative Stress: A Unifying Paradigm in Hypertension. Can, *J. Cardiol*, **2020**, 36, 659-670.
54. Umebayashi R.; Uchida HA.; Okuyama Y.; Kakio Y.; Hanayama Y.; Shikata K.; Wada J., The clinical efficacy of angiotensin II type1 receptor blockers on inflammatory markers in patients with hypertension: A multicenter randomized-controlled trial; MUSCAT-3 study, *Biomarkers*, **2019**, 24, 255–261.
55. Wu H.; Xu B., Inhibitory effects of onion against α-glucosidase Activity and its correlation with phenolic antioxidants, *Int J Food Prop*, **2014**, 17, 599–609.
56. Xanthis V.; Fitsiou E.; Voulgaridou G.; Bogadakis A.; Chlichlia K.; Galanis A.; Pappa A., Antioxidant and Cytoprotective Potential of the Essential Oil Pistacia lentiscus var. chia and Its Major Components Myrcene and *a*-Pinene, *Antioxidants*, **2021**, 10, 1-19.
57. Xia L.; Guo Q.; Tu P.; Chai X., The genus Casearia: a phytochemical and pharmacological Overview, *Phytochem Rev.*, **2014**.
58. Xu X.; Liu A.; Hu S.; Ares I.; Martínez-Larra˜naga M.; Wang X.; Martínez M.; Anad´on A.; Martínez M., Synthetic phenolic antioxidants: Metabolism, hazards and mechanism of action, *Food Chem.*, **2021**, 353, 1-15.
59. Yaribeygi H.; Maleki M.; Sathyapalan T.; Jamialahmadi T.; Sahebkar A., Anti-inflammatory potentials of incretin based therapies used in the management of diabetes. Life Sci. 2020;241: 117152.
60. Yaribeygi H, Maleki M, Sathyapalan T, Jamialahmadi T, Sahebkar A. Antioxidative Potentials of Incretin-Based Medications: A, *Oxidat Med Cell Long*, **2021**, 1-9.
61. Li, K., Zhong, W., Li, P., Ren, J., Jiang, K. and Wu, W. Recent advances in lignin antioxidant: Antioxidant mechanism, evaluation methods, influence factors and various applications. *International Journal of Biological Macromolecules*, **2023**, *251*,125992.
62. Bešlo, D., Golubić, N., Rastija, V., Agić, D., Karnaš, M., Šubarić, D. and Lučić, B. Antioxidant activity, metabolism, and bioavailability of polyphenols in the diet of animals. *Antioxidants*, **2023**, *12*(6), p.1141.