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# Syringic acid: A promising phenolic phytochemical with extensive therapeutic applications

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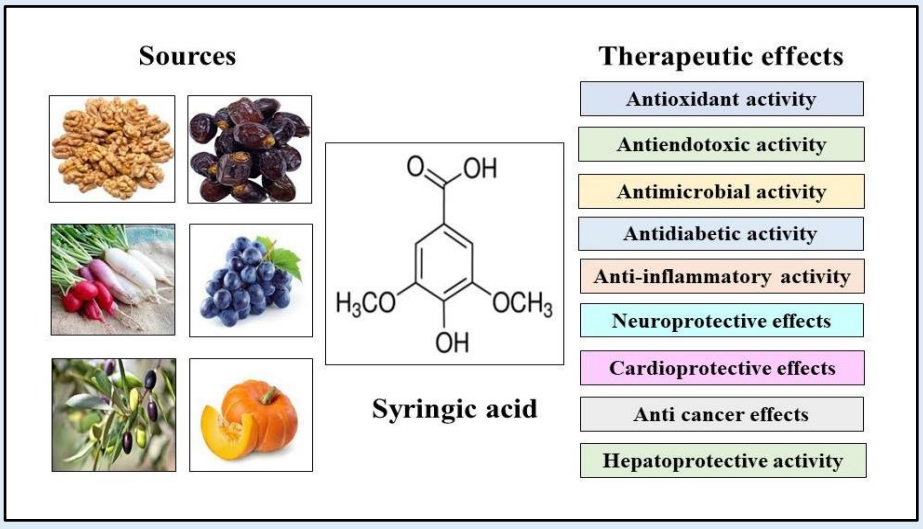
**ABSTRACT**

**Background:** Phenolic acids are bioactive phytochemicals that are pivotal in human health. Syringic acid is one of the most common phenolic acids and belongs to the class hydroxybenzoic acid. It is predominantly present in olives, dates, grapes, walnuts, radishes, and pumpkins. The chemical structure of Syringic acid consists of a benzene ring with a hydroxyl (-OH) group, one carboxylic acid group (-COOH) and two methoxy (-OCH3) groups attached to the ring. The methoxy groups' presence on the aromatic ring at positions 3 and 5 is responsible for conferring the therapeutic properties of Syringic acid. Syringic acid displays a diverse range of pharmacological properties, including antioxidant, anti-inflammatory, hepatoprotective, cardioprotective, neuroprotective, antimicrobial, antidiabetic, and antiendotoxic properties. This review aims to explore the natural sources, structure, biosynthesis, bioavailability, and therapeutic effects of Syringic acid.




**Graphical abstract:**

**Keywords:** Phytochemicals, Syringic acid, Bioactive compounds, Therapeutic effects



## INTRODUCTION

Plants play a vital role in both traditional and contemporary medicine, providing a rich variety of therapeutic compounds that can be utilized for a range of health benefits. Phytotherapy, accessible and culturally embraced as a healthcare approach, demonstrates cost-effectiveness and is significant in addressing numerous chronic non-communicable diseases. The protective benefits of plant-derived products arise from their diverse components, with unique mechanisms of action. These components include enzymes, proteins, and low molecular weight compounds such as vitamins, carotenoids, flavonoids, anthocyanins, and phenolic compounds. These phytochemicals are beneficial primarily due to their antioxidant properties, which help mitigate complications arising from oxidative stress [1, 2]. As a result, these organic molecules emerge as a promising reservoir for uncovering new therapeutic compounds. Phytoconstituents show potential by interacting with multiple pathways simultaneously. Different phytochemicals offer unique properties and benefits, and their effectiveness can vary depending on the context of use and the specific health condition being targeted.

Diet and functional foods have surfaced as effective approaches for preventing and managing various illnesses [3]. Functional foods are natural or processed food items containing known or unidentified biologically active compounds. When used in safe amounts, these substances have shown scientifically validated health advantages in preventing, managing, or treating chronic diseases [4]. Bioactive compounds found in functional foods contribute to their therapeutic effectiveness [5]. Exploring bioactive compounds in plant-based foods aims to grasp their biological effects in the human body, fostering the rise of functional foods as promising solutions for preventing and treating various illnesses [6].

Phenolic acids, a class of secondary metabolites, are commonly found in various plant species. They can be classified into two groups based on their chemical structure: hydroxybenzoic acids and hydroxycinnamic acids [7]. Hydroxycinnamates, also known as hydroxycinnamic acids (HCAs), consist of an essential chemical backbone characterized by a phenylpropanoid C6-C3 structure. Most hydroxybenzoic acids (HBAs) are characterized by a C6-C1 backbone directly derived from benzoic acid (BA). Examples include salicylic acid (SA), p-hydroxybenzoic acid (p-HBA), 2,5-dihydroxybenzoic acid (2,5-DHBA), 3,4-dihydroxybenzoic acid (3,4-DHBA), 2,3-dihydroxybenzoic acid (2,3-DHBA), 3,5-dihydroxybenzoic acid (3,5-DHBA), gallic acid (GA), and vanillic acid [8]. Phenolic acids are readily absorbed by the intestinal tract and provide health benefits by acting as potent antioxidants. Regular consumption of phenolic acids enhances the body's anti-inflammatory capabilities [9]. Apart from their antioxidant properties, phenolic acids demonstrate a spectrum of health-protective effects, encompassing antimicrobial, anticancer, anti-inflammatory, and anti-mutagenic activities [10].

Syringic acid is one of the prominent phenolic acids found in various plant sources. Syringic acid (SA), chemically known as O-methylated trihydroxy benzoic acid or 4-hydroxy-3,5-dimethoxybenzoic acid, is a naturally occurring phenolic compound. It is commonly found in various fruits and vegetables, including olives, grapes, walnuts, dates, radishes, and pumpkins [11].

Additionally, Syringaldehyde, a natural derivative of Syringic acid, is found in grapes and red wine [12]. Syringic acid has also been identified in certain pharmacologically significant fungal species, such as *Inonotus obliquus* and *Elaphomyces granulatus* [13, 14]. SA is also detected in extracts obtained from the stems and leaves of Bougainvillea [15].

Syringic acid demonstrates potent free radical scavenging properties, effectively mitigating oxidative stress markers. Its diverse therapeutic applications encompass preventing conditions such as diabetes, cardiovascular diseases (CVDs), cancer, and cerebral ischemia. Furthermore, it exhibits antioxidant, antimicrobial, anti-inflammatory, antiendotoxic, neuroprotective, and hepatoprotective activities, highlighting its multifaceted potential in promoting health and combating various ailments [11, 16, 17]. The biomedical effects of Syringic acid can be credited to its robust antioxidant potential, which stems from the presence of a phenolic structure containing various functional groups. Additionally, Syringic acid holds significance in the industrial sector as it is a component of lignin, a crucial constituent of plant cell walls. It is a vital substrate for fungal laccase enzymes, playing a substantial role in bioremediation and the pulp industry [18]. Moreover, owing to its reducing properties, Syringic acid is valuable as a component in dental resins in stomatology [19]. This review provides updated insights into the therapeutic properties of Syringic acid (SA), covering its sources, chemistry, biosynthesis, and therapeutic properties.

**Methodology:** A comprehensive electronic search was performed for studies published prior to February 2024, utilizing multiple databases, including PubMed, SCOPUS, Web of Science, Elsevier, ScienceDirect, ResearchGate, Google, and Google Scholar. Keywords related to syringic acid combined with terms such as structure, sources, antioxidant, anti-diabetic, anticancer, antimicrobial, anti-inflammatory, and hepatoprotective were employed in the search strategy.

**Structure of Syringic Acid**: The SA seed composition comprises a benzene ring connected to two $OCH_3$ (methoxy) groups, one OH (hydroxyl) group, and one COOH (carboxylic acid) group. The bioactivity of SA is impacted by the presence of these functional groups, especially the methoxy moieties attached to the aromatic ring at positions 3 and 5 [20]. The free radical-scavenging abilities of phenolic acids depend on the number of hydroxyl groups attached to the aromatic ring of benzoic or cinnamic acid molecules. Among various phenolic acids, (SA) has demonstrated more activity than its counterparts. The structure of Syringic acid is given in Figure 1. The sources of Syringic acid are shown in Figure 2.

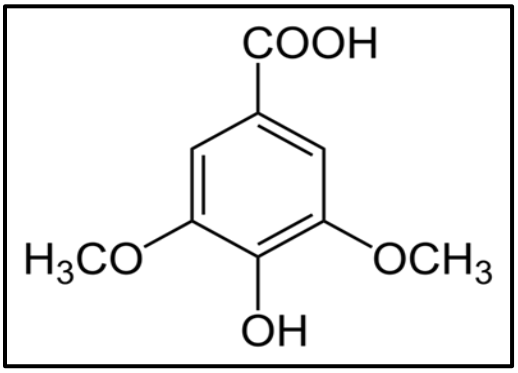



**Figure 1.** Structure of Syringic acid

| **Molecular formula** | **$C_9H_{10}O_5$** |
|---|---|
| **Molar mass** | 198.17 g/mol |
| **Boiling point** | 379.5$^0$C at 760 mmHg |
| **Melting point** | 205-209$^0$C |
| **Density** | 1.34 g/cm$^3$ |

**Table 1.** Properties of Syringic acid

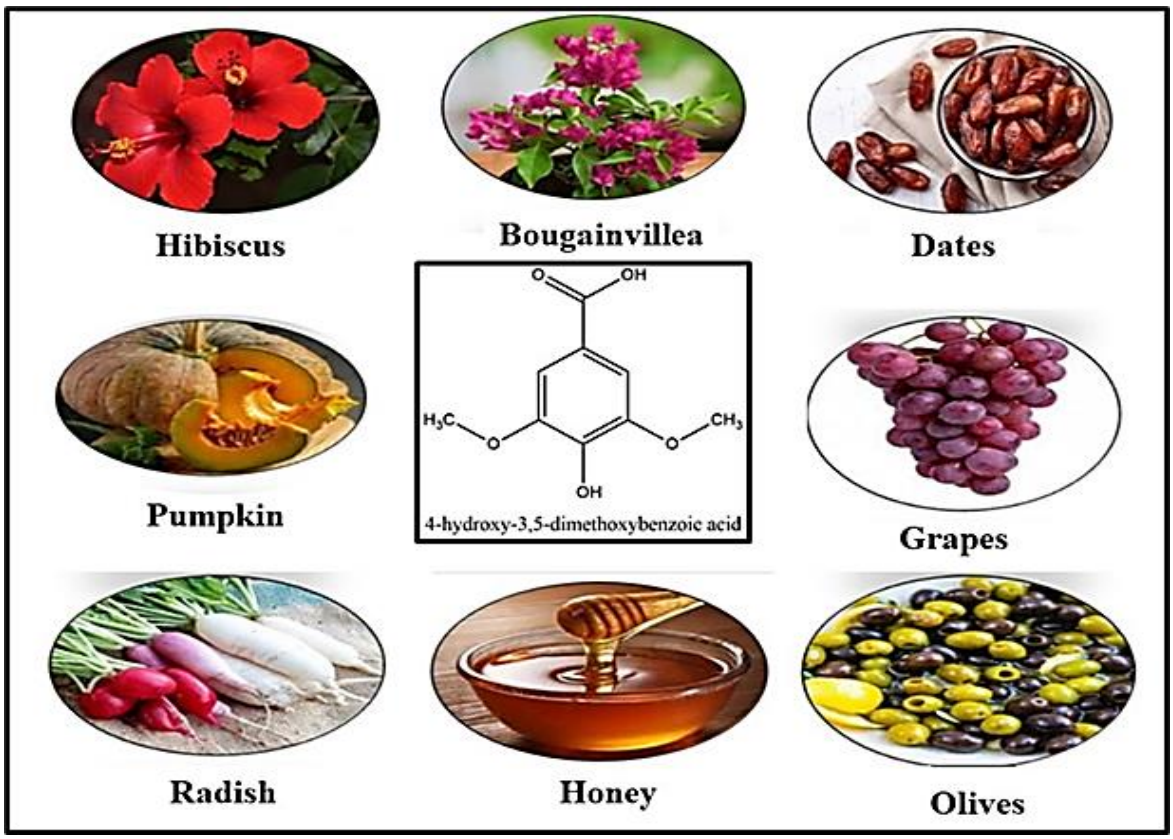



**Figure 2.** Sources of Syringic acid

**Biosynthesis of Syringic Acid:** SA is synthesized via a sequence of enzymatic reactions within plants, following the shikimic acid pathway. Alongside SA, this pathway generates intermediate phenolic compounds like protocatechuic acid, gallic acid, and quinic acid [21]. Syringic acid biosynthesis typically starts with the amino acid phenylalanine. Phenylalanine acts as a precursor for numerous phenolic compounds in plants. It undergoes conversion into cinnamic acid catalyzed by the enzyme phenylalanine ammonia-lyase (PAL). This step is a key entry point into the phenylpropanoid pathway. Cinnamic acid is hydroxylated to form p-coumaric acid, a process catalyzed by the enzyme cinnamate 4-hydroxylase (C4H). Sinapic acid can be formed from p-Coumaric acid in two

ways. Firstly, p-Coumaric acid undergoes activation to p-coumaroyl CoA catalyzed by 4-coumarate: CoA ligase (4CL). Then, coniferaldehyde is produced from p-coumaroyl CoA through the combined actions of cinnamoyl-CoA reductase (CCR) and cinnamyl alcohol dehydrogenase (CAD). Coniferaldehyde is further converted to sinapaldehyde, typically through the action of coniferaldehyde 5-hydroxylase (C5H). Sinapaldehyde is then converted to sinapic acid, a process catalyzed by sinapaldehyde dehydrogenase. In the alternate pathway, p-Coumaric acid is transformed into caffeic acid, subsequently converting to ferulic acid. Ferulic acid undergoes conversion to 5-hydroxy ferulic acid facilitated by ferulate-5-hydroxylase. 5-Hydroxy ferulic acid is then converted to Sinapic acid. Sinapic acid is methylated to form Syringic acid. The methylation step is carried out by the enzyme O-methyltransferase [22, 23].

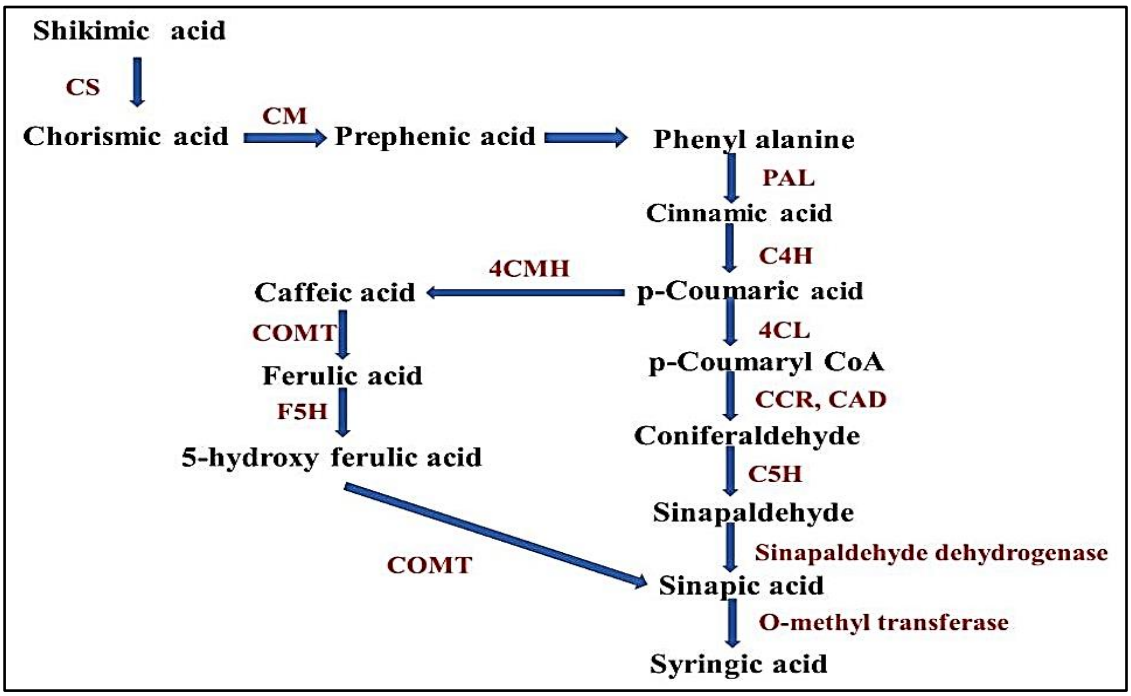



**Figure 3.** Biosynthetic pathway of Syringic acid

**Pharmacological Effects of Syringic Acid**: Syringic acid exhibits a diverse array of pharmacological properties, including potent antioxidant, antiproliferative, antiendotoxic, antimicrobial, anti-inflammatory, and anticancer effects [22, 24]. Syringic acid regulates oncogenic transcription factors and triggers apoptosis in cancer cells. Additionally, it demonstrates mitogenic properties and enhances chemosensitivity in human colorectal cancer cells [25]. Evidence suggests that syringic acid can potentially normalize hyperglycemia and ameliorate glycoprotein component abnormalities [26]. SA can protect against cerebral ischemia caused by blood deprivation by reducing oxidative stress and neuronal degeneration in rats [27].

**Antioxidant activity:** The biomedical advantages of SA can be credited to its strong antioxidant properties, which stem from its phenolic core adorned with diverse functional groups. Studies strongly endorse the consistent consumption of SA to afford substantial

protection against a spectrum of diseases linked to oxidative stress. Certain studies suggest that syringic acid lowers oxidative stress and protects against acute pancreatitis brought on by L-arginine [28]. SA has demonstrated antioxidant activity by effectively scavenging 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals [29]. There are reports that syringic acid outperformed ascorbic acid in anti-apoptotic, anti-inflammatory, and antioxidative properties. In rats with DMN-induced hepatotoxicity, this is accomplished by maintaining endogenous antioxidants and lowering the expression of pro-inflammatory and apoptotic markers [16]. Syringic acid treatment resulted in elevated levels of enzymatic (SOD, CAT) and non-enzymatic (GSH) antioxidants compared to the asthmatic control group in the mice model of asthma, highlighting the robust antioxidant response induced by Syringic acid [30]. Studies indicate that the scavenging activity of syringic acid against the HOO• radical is 1.53 times higher than that of ascorbic acid, making it a promising antioxidant [31].

**Anti-inflammatory activity:** Syringic acid has been reported to possess anti-inflammatory activity. Its mechanism of action involves the modulation of critical inflammatory signaling pathways and mediators. Specifically, Syringic acid has demonstrated the capability to regulate the NF-κB pathway (nuclear factor-kappa B), a pivotal factor in the expression of pro-inflammatory genes. Moreover, it has been reported to influence enzymes such as iNOS (inducible nitric oxide synthase) and COX-2 (cyclooxygenase-2), both integral to the inflammatory response. In rats with methyl cellosolve-induced hepato-testicular inflammation, Syringic acid exhibited anti-inflammatory effects by regulating the NF-κB-iNOS-COX-2 and JAK-STAT signaling pathways [32]. Pro-inflammatory cytokines are activated in response to various stimuli, aiming to safeguard host cells from damage, irritation, and infection. Notable examples of these cytokines include IL-1β, TNF-α, IL-6, and IFN-γ. There are reports that (SA) mitigates inflammatory responses induced by oxygen-glucose deprivation and reperfusion (OGD/R) by decreasing the levels of pro-inflammatory cytokines. The anti-inflammatory properties of syringic acid make it a subject of interest in various studies exploring natural compounds with therapeutic potential against inflammatory conditions [33].

**Anticancer effects:** Syringic acid has been studied for its potential anticancer effects, showing promise in inhibiting the growth and proliferation of cancer cells. Reports suggest that syringic acid effectively suppressed the proliferation of gastric cancer cells, alleviated inflammation, and triggered apoptosis in cancer cells. These effects were associated with the upregulation of mTOR through the AKT signaling pathway. Previous studies suggested that Syringic acid holds promise as a potential chemotherapeutic candidate for treating gastric cancer [34]. Administration of Syringic acid led to a notable dose-dependent inhibition of cellular proliferation. In addition, SA induced apoptosis by elevating cellular reactive oxygen species (ROS) and DNA damage levels, as well as downregulated essential proliferative genes. Administering syringic acid to rats with colorectal tumors resulted in a significant decrease in tumor volume and incidence [35]. In a previous study conducted by Lavanya et al., the therapeutic efficacy of Syringic acid (SA) was investigated in Wistar rats with induced hepatocellular carcinoma. The research illustrated that SA provided a protective effect against diethylnitrosamine (DEN)-induced hepatocellular carcinoma [36]. A study examining the Antitumoral

Activity of Syringic Acid on HT-29 cells revealed that Syringic acid exhibits therapeutic effects on colorectal cancer [37]. There are also reports that Syringic acid has the potential to induce cytotoxicity in the human hepatoma HepG2 cell line through reactive oxygen species-mediated mechanisms [38]. Syringic acid exerted inhibitory effects on the proliferation, invasion, and migration of glioblastoma cells by suppressing the expression of matrix metalloproteinases, ultimately promoting apoptosis [39].

**Antimicrobial activity**: Phenolic compounds, both natural and synthetic, are being explored for their potential use in food preservation, pharmaceuticals, and other applications where antimicrobial properties are desirable. The antimicrobial activity of phenolic compounds can vary depending on factors such as the specific compound, concentration, and the type of microorganism targeted. Syringic acid has also been investigated for its potential antimicrobial properties. The phenolic structure of syringic acid (SA) imparts antimicrobial activity against a variety of microorganisms. Studies have indicated that SA, extracted from diverse mushroom species, exhibits antibacterial effects against both Gram-negative and Gram-positive bacteria. Research investigating the antimicrobial potential of syringic acid against *Cronobacter sakazakii* demonstrated its ability to impede bacterial growth. This effect was accompanied by disruptions in cell membrane functionality, evidenced by a decrease in intracellular ATP concentration, a reduction in intracellular pH, hyperpolarization of the cell membrane, and alterations in cellular morphology. These results suggest that syringic acid holds promise for development as a natural preservative to manage *Cronobacter sakazakii* in food products, thereby aiding in the prevention of related infections [40]. Syringic acid possesses the capability to combat biofilms formed by methicillin-resistant *S. epidermidis* bacterial strains. Combined with antibiotics, it can potentially reduce the prevalence of nosocomial infections [41].

**Hepatoprotective effects**: Syringic acid has been investigated for its hepatoprotective effects, indicating its potential to safeguard the liver from various insults and damage. Syringic acid could effectively hinder the activation of cultured hepatic stellate cells, which are pivotal contributors to liver fibrogenesis. The administration of Syringic acid demonstrated the capacity to mitigate hepatic fibrosis in the context of chronic liver injury [42]. The investigation into the impact of Syringic acid (SA) on acetaminophen (APAP)-induced hepatotoxicity in rats demonstrated that Syringic acid effectively reduced lipid peroxidation markers while enhancing the activity of enzymatic antioxidants in the liver. These results show that Syringic acid significantly protects against APAP-induced hepatic injury in rats [43]. Syringic acid exhibits hepatoprotective effects against hepatic encephalopathy by alleviating hepatotoxicity biomarkers. It exhibits antioxidant and anti-inflammatory characteristics, as well as effectively controlling hyperammonemia [44]. Cirrhosis and hepatocellular carcinoma stand as the leading causes of mortality in individuals with diabetes. Reports indicate that Syringic acid can potentially alleviate hepatic damage caused by chronic hyperglycemia in Wistar rats [17]. Syringic Acid (SA) exhibited robust hepatoprotective effects against depletion of endogenous antioxidant enzymes induced by Methyl cellosolve (MECE). It also hindered MECE-induced cytosolic Nrf2 activation and the inhibition of antioxidant response element (ARE)-dependent genes in rats [45]. Reports show that SA can effectively inhibit

Sodium valproate-induced hepatotoxicity, attributed to its potential anti-inflammatory effects [46].

**Cardioprotective effects**: In various studies, syringic acid has been found to exhibit cardioprotective effects. These protective effects are attributed to its ability to modulate several physiological processes and mechanisms within the cardiovascular system. Despite numerous advancements in the treatment of ischemic heart disease, myocardial infarction (MI) remains a significant health concern, continuing to warrant significant attention and research efforts from the scientific community. In a rat model of isoproterenol-induced myocardial infarction (MI), Syringic Acid (SA) demonstrated cardioprotective potential. The study results indicated that this protective effect could be attributed to the anti-lipid peroxidative properties of SA and its enhancement of the endogenous antioxidant system [47]. By reducing lipid peroxidation and protein carbonyl content, SA therapy demonstrated protective effects in rats with diabetic cardiomyopathy. The potential mechanisms underlying these effects are likely linked to the antioxidant activity of this phenolic acid. SA may serve as a protective factor against cardiac challenges associated with diabetes [48]. Syringic acid demonstrated the ability to inhibit apoptosis pathways in H9c2 cardiomyocytes subjected to hypoxia/reoxygenation injury by downregulating the p38MAPK and JNK signaling pathways [49]. Earlier investigations led by S Manjunatha *et al.,*2020 unveiled the synergistic cardio-protective potential of Syringic acid and resveratrol against isoproterenol-induced cardiotoxicity in rats by mitigating NF-kB and TNF-α pathways [50]. One of the main risk factors for cardiovascular disease development is hypertension. In rats with hypertension brought on by N-nitro-L-arginine methyl ester (L-NAME), Syringic acid exhibited antihypertensive efficacy [51]. SA has demonstrated protective effects against ischemia/reperfusion injury, where restoring blood flow after a period of ischemia can lead to tissue damage [52]. This protective action is crucial for maintaining cardiac function. The available evidence indicates that Syringic Acid, with its antioxidant, anti-inflammatory, anti-apoptotic, and pathway-regulating attributes, shows potential as a cardioprotective compound. Obesity is a significant contributing factor in the development of cardiovascular diseases. Syringic acid inhibits adipogenesis and boosts lipolysis in 3T3-L1 adipocytes, resulting in reduced lipid accumulation and diminished ROS accumulation. These findings suggest that SA has anti-obesity effects *in vitro* [53].

**Neuroprotective effects:** Phenolic phytochemicals have demonstrated promising neuroprotective effects through multiple mechanisms. These compounds, including flavonoids, phenolic acids, and polyphenols, have been associated with preserving neurological function and preventing neurodegenerative diseases. Neurodegenerative disorders, including Alzheimer's disease (AD), Parkinson's disease (PD), traumatic nervous system disorders, dementia, and various neurological conditions, impact hundreds of millions of people worldwide. Syringic Acid (SA) has demonstrated a significant impact on excitatory neurotransmitters, contributing to the alleviation of behavioral dysfunctions. SA treatment holds the potential for managing neurological dysfunction and behavioral impairments, primarily due to its antioxidant and anti-inflammatory properties. Moreover, the effectiveness of SA in treating neurological diseases is likely contingent on factors such as administration method and appropriate dosage [54].

There are other reports that SA, via reducing cell injury caused by oxygen-glucose deprivation/reoxygenation (OGD/R), displayed strong neuroprotective benefits in hippocampus neuronal cells. These effects are likely mediated through the attenuation of the JNK and p38 signaling pathways [55]. The oral administration of SA resulted in significant neuroprotective effects against sub-chronic deltamethrin intoxication. SA mitigated the severity of DTM-induced effects on biochemical and histopathological parameters and demonstrated antioxidant properties.

SA therapy appeared to inhibit apoptosis of CA1/3 pyramidal neurons, degenerative cellular disarray, and oxidative damage caused by reactive oxygen species and reactive nitrogen species (ROS/RNS) [56]. Syringic Acid has a neuroprotective effect by modulating the oxidative stress and mitochondrial mass in diabetic rats [57]. Syringic acid also demonstrated neuroprotective effects against oxidative stress-mediated neuroinflammation induced by aluminum chloride in a rat model of Alzheimer's disease [58].

**Antidiabetic effects**: Syringic acid has been shown to ameliorate hyperglycemia in experimental diabetic rats [26]. It has exhibited an antihyperglycemic effect by mitigating the activity of crucial enzymes involved in carbohydrate metabolism in these rats [59, 60].

One major issue that is becoming more common in people with diabetes is diabetic cardiomyopathy or DC. In streptozotocin-induced diabetic rats, syringic acid has demonstrated the ability to alleviate cardiomyopathy [48]. It has been reported to demonstrate nephroprotective effects in diabetic rats, particularly in the context of diabetic nephropathy, a condition that can lead to renal diseases [61]. SA provides antioxidant protection in the pancreas of type 2 diabetic rats by restoring the antioxidant defense system [62]. Syringic acid mitigated experimental diabetic nephropathy in rats by exerting anti-inflammatory, antioxidant, and anti-fibrotic effects. These beneficial effects were achieved by suppressing the Toll-like receptor-4 pathway [63]. Syringic acid promoted the regeneration of β-cells and alleviated alloxan-induced pancreatic damage in diabetic rats [59]. Studies suggest that the anti-diabetic effects of syringic acid (SA) could be either increased insulin release from pancreatic β-cells or increased utilization of glucose by peripheral tissues [22]. Syringic acid aids in mitigating diabetic kidney disease by modulating oxidative stress and autophagy mechanisms [64].

**Antiendotoxic activity**: Antiendotoxic activity refers to the ability of a substance, such as a drug or a natural compound, to counteract or mitigate the toxic effects of endotoxins. Endotoxins are toxic substances produced by certain bacteria, particularly Gram-negative bacteria, released upon bacterial cell lysis or destruction. Lipopolysaccharide (LPS) is a common example of an endotoxin found in the outer membrane of Gram-negative bacteria. Syringic acid has been reported to exhibit antiendotoxic activity, suggesting its potential to mitigate the effects of endotoxins in biological systems. Research on the anti-endotoxic properties of SA extracted from *Radix Isatidis* (Banlangen, BLG) demonstrated that pretreatment with SA resulted in the destruction of 83.16% of endotoxins (ET)[65]. The possible mechanisms of therapeutic action of Syringic acid are shown in Figure 4.

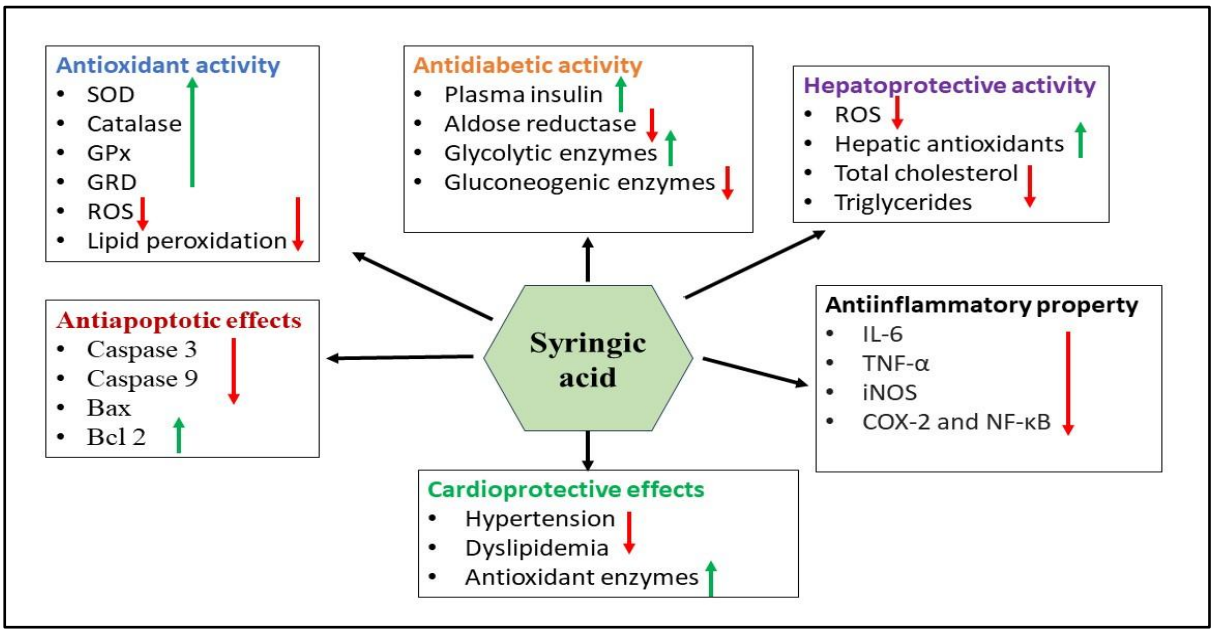



**Figure 4.** The possible mechanisms of therapeutic action of Syringic acid

**Bioavailability of Syringic Acid:** Bioavailability refers to the extent to which an active compound or drug reaches the bloodstream and becomes accessible at the intended site of action. The concentration of the drug available at the target site can serve as a reliable indicator of its bioavailability. However, this measure can be influenced by several physical and chemical factors during systemic circulation. The bioavailability of syringic acid can vary depending on factors such as the route of administration, formulation, and individual differences in absorption and metabolism. However, studies have indicated that Syringic acid exhibits relatively high bioavailability in various experimental models. The pharmacokinetics and bioavailability study conducted on rabbits showed that the absolute bioavailability of syringic acid was 86.27% [66]. Studies have demonstrated that loading syringic acid onto TPGS liposomes can enhance its oral bioavailability and in vivo antioxidant efficiency [67].

## CONCLUSION

Syringic acid is a phenolic phytochemical found in various plant sources, garnering attention for its diverse therapeutic applications due to its beneficial properties. As an antioxidant, it helps combat oxidative stress by scavenging free radicals in the body, which is crucial for preventing cells and tissues from oxidative damage. Syringic acid exhibits anti-inflammatory effects, which may aid in managing many diseases by modulating inflammatory pathways. Research suggests that syringic acid may have anti-diabetic effects, influencing insulin release and enhancing glucose utilization by peripheral tissues. This potential makes Syringic acid a candidate for managing diabetes and its complications. Additionally, syringic acid possesses potent hepatoprotective, neuroprotective, anticancer, and antimicrobial properties. In summary, the multifaceted therapeutic applications of syringic acid, including its antioxidant and anti-inflammatory effects and its influence on various physiological systems, make it a promising phytochemical for potential use in health and disease management. However, more investigation and clinical trials are required to completely comprehend its mechanisms of action and determine the ideal circumstances for therapeutic application. In addition, consuming Syringic acid in the form of whole foods rather than isolated

supplements may offer additional health benefits due to the synergistic effects of other compounds in those foods.

**Abbreviations:** APAP- Acetaminophen, ARE-antioxidant response element, CAD-cinnamyl alcohol dehydrogenase, CCR- cinnamoyl-CoA reductase, C4H-Cinnamate 4-hydroxylase, C5H- Coniferaldehyde 5-hydroxylase, CAT-catalase, DPPH- 2,2-diphenyl-1-picrylhydrazyl radicals, DTM- Deltamethrin, GPx-Glutathione peroxidase, GRD- Glutathione reductase, LPS- lipopolysaccharides NF-κB -nuclear factor-kappa B, OGD/R- oxygen-glucose deprivation/reoxygenation, PAL-phenylalanine ammonia-lyase, SA-Syringic acid, SOD-Superoxide dismutase

**Authors' contributions:** S Shimsa and S Mini authored the full text of the review article. Sukanta Mondal wrote and edited the article in part, which S Mini revised. All authors wrote and edited the final draft. All others participated in data collection and revised the article critically for important intellectual content.

**Competing interests:** The authors have no financial interests or conflicts of interest.

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