Biomedicine & Pharmacotherapy 108 (2018) 547–557

Contents lists available at ScienceDirect

Biomedicine & Pharmacotherapy

journal homepage: www.elsevier.com/locate/biopha

# Syringic acid (SA) – A Review of Its Occurrence, Biosynthesis, Pharmacological and Industrial Importance

Srinivasulu Cheemanapalli[a,*], Ramgopal Mopuri[b], Ramanjaneyulu Golla[c], Anuradha C.M.[b], Suresh Kumar Chitta[a]

[a] Department of Biochemistry, Sri Krishnadevaraya University, Anantapuramu 515003, A.P., India
[b] Department of Biotechnology, Sri Krishnadevaraya University, Anantapuramu 515003, A.P., India
[c] Biochemistry division, CSIR-CIMAP Research Centre, GKVK post, Bangalore-65, K.A., India

ARTICLE INFO

*Keywords:*
Syringic acid
anti-oxidant
cancer
diabetes
bioremediation
laccase

ABSTRACT

The use of phytochemicals in control of human diseases have been considerable public and scientific interest in current days. Syringic acid (SA), a phenolic compound often found in fruits and vegetables and which is synthesized via shikimic acid pathway in plants. It shows a wide range of therapeutic applications in prevention of diabetes, CVDs, cancer, cerebral ischemia; as well as it possess anti-oxidant, antimicrobial, anti-inflammatory, antiendotoxic, neuro and hepatoprotective activities. It has an effective free radical scavenger and alleviates the oxidative stress markers. The therapeutic property of SA is attributed by the presence of methoxy groups onto the aromatic ring at positions 3 and 5. The strong antioxidant activity of SA may confer its beneficial effects for human health. SA has the potential to modulate enzyme activity, protein dynamics and diverse transcription factors involved in diabetes, inflammation, cancer and angiogenesis. *In vivo* experimental data and histopathological studies on SA activity has delineated its possible therapeutic mechanisms. Besides usage in biomedical field, SA has greater industrial applications in bioremediation, photocatalytic ozonation, and laccase based catalysis. The present review deals about SA natural sources, biosynthesis, bioavailability, biomedical applications (*in vivo* and *in vito*. The review addresses basic information about molecular mechanisms, therapeutic and industrial potential of SA.

## 1. Introduction

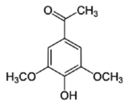
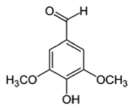
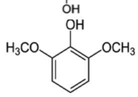
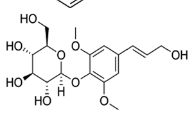
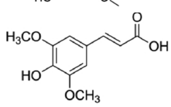
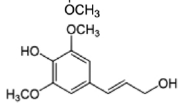
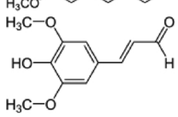
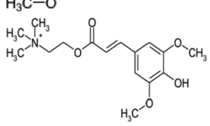
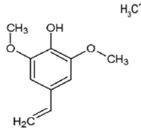
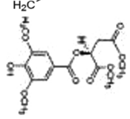
Polyphenols are the good antioxidants, which occur in fruits and vegetables. Among polyphenols (flavonoids, stilbenes, phenolic acids and lignans), the phenolic acids are major constituents in plant kingdom, which shares similar structural features as well as functional groups [1]. The natural antioxidants have tend to suppress oxidative stress and neutralize free radicles generated in the biological systems [2]. Anioxidant potential of natural compounds confers its therapeutic activities for wide variety of diseases such as CVDs, cancer, liver diseases, diabetes, and neurodegenerative disorders [3–5]. There has been increased public and scientific interest in the use of natural antioxidants instead of synthetic agents [6–8]. Structural diversity of antioxidants gives certain properties such as reducing agents, metal chelators, free radical scavengers, enzyme modulators and regulators of diverse proteins and transcriptional factors [9].

SA is one of the abundant phenolic compound present in olives, dates, spices, pumpkin, grapes [10], acai palm [11], honey, red wine and other plants. SA exhibits useful properties in biomedical sector such as anti-oxidant, anti-microbial, anti-inflammation, anti-cancer, anti-diabetic and protection of the heart, liver and brain/CNS [12]. Along with clinical usage, SA has greater importance in the industrial sector. Lignin (plant cell wall component) is made up of abundant aromatic compounds in nature. Along with other phenolic compounds, SA is also contributing to the structural integrity of the lignin. The presence of SA in the lignin may acts as a good substrate for the fungal laccase enzyme, which has greater importance in bioremediation and pulp industry [13]. Owing to it's caries-reducing property, SA has been employed in the preparation of dental cement [14]. SA based synthetic lignin-polymers are prepared by using laccase catalyzed polymerization [15]. The present review updates the therapeutic properties of SA and provides its sources, chemistry, biosynthesis, molecular mechanism of action in various diseases.

* Corresponding author.
*E-mail address:* srenubio@gmail.com (C. Srinivasulu).

https://doi.org/10.1016/j.biopha.2018.09.069
Received 4 August 2018; Received in revised form 10 September 2018; Accepted 11 September 2018

**Table 1**
Naturally occurring syringic acid (SA) derivatives

| S. No | Name | Chemical structure | Occurrence | Importance |
|---|---|---|---|---|
| 1 | Acetosyringone |  | Wide variety of plants | Plant-pathogen recognition [123] |
| 2 | Syringaldehyde |  | Cell walls of plants | Food and cosmetic industries [124] |
| 3 | Syringol |  | Wood smoke | Smoke flavor in foods [125] |
| 4 | Syringin |  | Stem bark of *Magnolia sieboldii* and wide variety of plants | Antiinflammatory, antinociceptive [126] and antidiabetic effects [127] |
| 5 | Sinapinic acid |  | Fruits, vegetables, oilseeds, medicinal plants and cereal grains | Antioxidant, antimicrobial, anti inflammatory, analgesic, and anticancer [128] |
| 6 | Sinapyl alcohol |  | Cell walls of plants | Anti-inflammatory and antinociceptive effects [126] |
| 7 | Sinapaldehyde |  | Cell walls of plants | Antimicrobial, antioxidant [129] and prostaglandin synthetase inhibitor [130] |
| 8 | Sinapine |  | Seeds of the cruciferous species | Anti-inflammatory [131], antioxidant [132], anti-angiogenic and [133], anticancer effects [134] |
| 9 | Canolol |  | Crude canola oil | Antioxidant [135] and anticancer effects [136] |
| 10 | Stageobester A |  | Roots of *Stachys geobombycis* (family-Lamiaceae) | Antioxidant effects [137] |

## 2. Occurrence

SA has distributed in wide variety of plant products (fruits and vegetables) and certain fungal species. At the same time SA possesses its natural derivatives (Table 1), which are occuring along with SA in plants. SA is identified in floral honeys and which may provide antioxidant property of honey [16–17]. Total percentage of phenolic compounds are estimated in honey is 1.5-4.2%; they are SA, gallic acid, p-coumaric acid, cinnamic acid, vanillic acid and caffeic acid [18]. Lignin is the waste product of pulping industry and it contains syringaldehyde (natural SA derivative) bioactive compounds. During the conversion process of biomass to ethanol, lignin used as a source of active compounds [19]. Syringaldehyde is also found in grapes and in red wines aged in wooden barrels [20–21]. In the same way syringaldehyde is also a constituent of wood smoke and smoke flavorings [22]. SA and other secondary metabolites are identified in extracts of stems and leaves of Bougainvillea [23]. The leaf extract of Bougainvillea has shown several pharmacological activities like antioxidant, anticancer, antibacterial, antiviral, and etc. All parts of the Bougainvillea plant include roots are used for medicinal purpose. In general, it is used as a tea for cough, fever, sore and diarrhea. SA isolated from the methanolic fraction of the galls of *Quercus infectoria,* which shown neuropharmacological activity in the laboratory mice and frogs. The experimental data has suggested that, presence of SA in *Q. infectoria* plant extract is responsible for its anesthetic and sedative activity [24].

The phytochemical screening of Paspalum scrobiculatum L (Kodo millet) contains phenolic compounds such as quercetin, ferulic acid, vanillic acid and SA [25]. The millet variety, *Paspalum scrobiculatum* was habituated in Asian and African countries and it has several pharmacological and nutraceutical importance. *P. scrobiculatum* have antifungal, antibacterial, antioxidant and antidiabetic activities [26]. The HPLC analysis of Ardisia crenata extract reported that presences of nine compounds (include SA) have been studied for anti-proliferative activity on MDA-MB-231 breast cancer cells [27]. Proso millet (*Panicum miliaceum* L.) is an important cereal, which contains valuable components of the human diet especially used in developing countries. Epidemiological studies have revealed that utilization of proso millet is connected with reduced risk of various long standing diseases. In proso millet constituents, SA was identified in free fraction [28]. SA presents profusely in cereals, for example: maize, oats, barley, rice, rye, wheat and sorghum [29]. SA plays an important role in the interaction between oil palm and *Ganoderma boninense*, which is causal agent of basal stem rot disease of oil palm. The presence of phenolic content in *G. boninense* infected and healthy oil palm roots have shown that, low phenolic content was observed in infected plant than healthy plants. It evidenced that phenolic compounds (include SA) are involved in oil palm resistance against *Ganoderma* [30–31]. SA, a metabolite of