IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, November 2022
Impact Factor: 6.252

Ellagic Acid: A Review on its Natural Source, Chemical Stability and its Derivatives

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Abstract: *Ellagic acid is a powerful bioactive compound with many potential pharamacological and industrial applications .in this review, the chemical aspects, biological properties and diverse potential applications of ellagic acid for different industries were described. This reviw also discussed the advance in ellagitann in biodegradation, focusing on the process of isolation of microorganism and strain selection, medium and culture optimization, as well as fermentation system for commercially viable industrial scale production. The performances of various fermentation techniques that have been applied for the production of ellegic acid from residual by products were compared, while the advantages and disadvantages of each plant source were also discussed.*

Keywords: Ellagic acid, ellagitannin, biodegradation, fungal physiology, solid state fermentation, submerged fermentation

I. INTRODUCTION

Plant polyphenols are the most comman and abundant phytochemicals that are biosynthesized through shikimate derived phenylpropanoid and polyketide pathways [1]. Tannins are an important group of polyphenols that are classified into two board categories hydrolysable tannins that encompass polymers of Gallic or ellagic acid [EA] and are esterconnected with a sugar residue, and condencsed tannins also known as proanthocyanidins which are carbon-carbon linked polymers of flavan-3-ols [2]. Ellagic acid is found in free and glycosylated forms, or in the form of complex polymers esterified with a sugar called ellagitannins [ETs] [3]. Ellagic acid has received considerable research attention owing to its pharmacological effect that are relevant to the treatment of chronic diseases [4]. This review focuses on the chemistry and main biological properties of EA, and the mechanisms responsible for the pharmacological effect of this phytochemical. [5]

Chemistry of ellagic acid [EA]

Ellagic acid [EA], first noticed by chevreul in the gallnut, was described in 1818 by braconnot, who named the acid by reversing the word Galle [6]. EA is consist of a dimeric derivative of gallic acid with molecular weight of 302.194g/mol. According to IUPAC nomenclature, EA is identified as 2,3,8,7 tetra-hydroxychromino [5, 4, 3-cde] chromene-5,10dione, though the most comman designation in chemistry may be found based on diphenic acid classification.EA comprises four free OH group and two acyloxy group linked to core of fused aromatic rings, keeping a near planar structure with molecular symmetry crystallizing in the monoclinic cell, space group P2/c [7]. EA can be partially or fully ionized, suggesting that ions could also be involved in the antioxidant activity and underlining the importance of EA protolytic equilibria studies. All four phenolic groups can suffer deprotonation, which would suggest four Pka valueassigned to 4-4'-OH and 5-5'-OH are referred. Simi and co-workers [8].

Free radical scavenging activity of EA relates to the phenolic H-atom transfer, single electron transfer followed by proton transfer [SET-PT], and sequential proton loss electron transfer [SPLET] mechanisms. By analyzing the energy requirements for the bond dissociation enthalpy [BDE] adiabatic ionization potential [IP], O-H proton dissociation enthalpy, proton affinity and electron transfer enthalpy, it is possible to inidicate which mechanism is

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thermodynamically favoured and identify the activity site for radical inactivation [9]. The oxidative C-O coupling between galloyl and hexahydroxydiphenoyl moieties, ET monomers can form dimers, trimers and tetramers with molecular weight up to several thousands of DA Eg.Sanguine H-6, a casuarictin dimer, the natural of bond between monomers, either biphenyl or diarylether, sets up a method for their classification [10]. Lastly, ETs can give rise to hybrid structures by joining with other classes of molecules,Eg; Epiacutissimin B, flavanol-ellagitannin, has epicatechin at the C-1 center of the open-chain glucose core [11].

II. SOURCES OF ELLAGIC ACID

ETs are known constituents of numerous species of economic importance, they are abundant in berries of the family rosaceae such as cloudberry, raspberry and strawberry. They seem to have most of their EA in the form of ETs, as the relative amount of free EA and its glycosides is rather low [12]. In general, the amount of EA/ET in fruit can range from 100 to 1500mg.kg and contributes substantially to the dietary intake, Kakadu plum, with up 140.2g.kg of EA, is probably the richest edible source [13]. EA, Methyl derivatives of EA, and glycosides of both, are the components of the tannin extractives of Eucalypyus species, therefore the EA, and is also present in agro-forest and industrial residues. [14]. The industrial importance of Eucalyptus species for cellulosic pulp production in south Europe, Australia, Asia, Sauth America, and South Africa predetermines a particular interest in these angiosperms, since eucalypt wood is used in pulping processes after the preliminary removal of bark, the letter can be considered as a large source of ETs as wel. EA is present in the different industrial stream from the production of boyh Kraft and sulphate pulps [15].

Production of Ellagic Acid

The recovery and isolation of bioactive phytochemicals from plant materials is usually carried out by employing various extraction procedures. The production of commercial EA is achived through extraction of the ET-rich plant fraction using acid methanol mixtures as solvent, followed by ETs hydrolysis to EA with concentrated HCL [16]. It must be noted that, despite being the preferred approaches to EA production, conventional extraction method are unselective, being affected by the large diversity of ET structures, a vast assortment of plant sources and a troubling purification thus, leading to low yield of EA, contaminations and excessive costs. Accordingly, there has been a need to develop alternative technologie, more efficient in term of yield and energy cost, in order to produce EA of higher purity and on a longer scale, ideally from sources that do not complete with the food processing industry therefore, biothechological production has emerged as a promising alternative, being the focus of many studie. EA can be produce from pomegranate ETs using ellagitannins or ellagic titanic acylhydrolase [17].

However, the use anzymatic method requires the optimization of production, extraction and enzyme purification. In fact, it is essential to optimize fermentation systems as there are certain limitation performance ratios of macro and microelements for a given culture media, hidden existence trace element and growth factors, and use of unconventional source of nutrients, among others. Nevertheless, several advances have been made. A possible pathway of ET biodegradation, and the production of EA from punicalagin, was proposed by acaciaValdes and co-authors [18]. The synthesis of ETs is much more complex than that EA, has relatively small yield and posses a major challenge, generating stereoselective linkages of galloyl-derived biphenyl moieties across different site of the glucose core nevertheles

Technical Application of Ellagic acid

More recently, wang and co-workers developed conductivity based sensors via the assembling of EA molecules through hydrogen bond between EA molecules. Due to the near planar structure of EA, the obtaind nanostructure exhibit a 1D dimensional structure, ehose conductivity and fluorescence selectively change in the presence of nitrobenzene, indicating the potential of these nanomaterial for the detection of explosive chemicals. EA and catechols, in combination with lignin, were reported as a part of all solid potentiometric chemical sensor for the selective detection of aqueous solution.[19] In order to enhance EA bioavilability and maximize its activity, attempts have been made to develop a delivery system using a chitosan polymer in composite films based on scaffolds and nanocapsules[20].

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Biological Functions of Ellagic acid

Free radical mediated oxidative damage of biological molecules has been associated with pathogenesis of several diseases and senescence physiological pathways [21]. Given their ability to quench free electrons, EA and ET can protect vital molecules from hazardous freeradicals [22]. Aditionally, due to structural similarities with several key signalling molecule, they can triggergene expression of molecule engaged in antioxidant defence. Similarly, they can repress the expression of protein, enzymes and transcription factor involved in oxidative stress producing pathways such as nicotinamide adenine dinucleotide phosphate oxidase and cytochrome P450[CYP]dependent phase-I enzyme. In such way, EA participates not only in the management of endogenous and exogenous source of reactive oxygen species but also in antioxidant defense mechanisms [23]. A more detailed overview of EAs antioxidant mechanisms and their link with multiple biological activities can be found in couple of recent reviews [24].

II. CONCLUSION

EAandits derivatives are natural bioactive compounds with significant beneficial health effects and potential for advanced technical applications. However, the expansion of application areas and the commercial exploration of EA are hampered by the lack of market availability of high-grade products. Accordingly, the wood processing sector, in particular by-products from the pulping industry, could be a valuable all-season source alternative to food competing crops. The detailed knowledge on structural changes of ETs and the composition of EA derivatives in industrial streams would be the first step towards a wider exploration in technical and biomedical applications.

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