Therapeutic Effects of Gallic Acid: Current Scenario

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Gallic acid (GA), a member of the hydroxybenzoic acids, is a naturally occurring substance found in oak bark, tea leaves, gall nuts, apple peels, sumac, green tea, wine and grapes [1]. GA is polyphenolic compound present in plants. It is found su ciently in berries, tea, grapes, and other fruits as well as in wine. is polyphenolic compound is also present in some hard wood plant species such as, oak (*Q erc s rob r*), chestnut (*Castanea sati a* L.) and many others. In human blood plasma, micromolar concentrations of free and glucuronidated forms of GA and its main metabolite 4-O-methylgallic have been found a er ingestion of GA-rich foods, this shows the good absorption property of GA [2]. Under acid hydrolysis of hydrolyzable tannins, GA could be obtained [3]. It is a yellowish white crystal with molecular mass 170.12 g/mol. Its melting point is 250°C and water solubility 1.1% at 20°C. GA could be formed from phenylalanine *ia* ca eic acid or 3,4,5-trihydroxycinnamic acid (route 1) by the use of intermediates of shikimate pathway. Gallic acid can also be derived directly from 5-dehydroshikimate by use of enzyme shikimate dehydrogenase (SDH) (route 2), by dehydrogenation or from protocatechuate as an intermediate (route 3) (Figure 1).

Many pharmacological and biochemical pathways are a ected by GA because of its strong anti-in ammatory, antioxidant, anticancer and antimutagenic properties [4] GA has been reported to prevent a number of disorders, including cardiovascular disease, cancer, in ammation, infection [5]diabetes [6], and neurological ailments [7].

GA, being a strong natural antioxidant, has the ability to remove reactive oxygen species (ROS), e.g., hydrogen peroxide, superoxide anions, hypochlorous acid and hydroxyl radicals. is antioxidant e ect could prove bene cial to many diseases [2]. Some GA derivatives such as methyl, propyl, octyl and dodecyl gallates as antioxidants, are widely used in food manufacturing, pharmaceutical and cosmetic industries. Pharmacokinetic and pharmacodynamic properties can be modi ed by inducing chemical changes in GA molecules which alter the solubility and the degree of ionization [3].

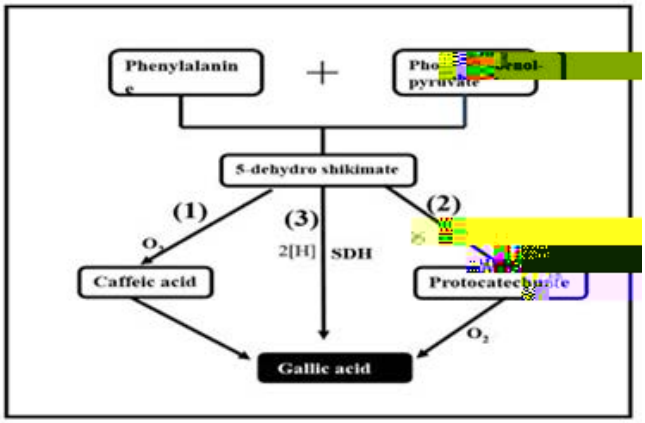

Figure 1: Pathways for Gallic acid biosynthesis.

is review systematically highlights the merits of GA as anti-cancer, anti-in ammatory, anti-diabetic,neuroprotective, and anti-hepatitis.

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Cancer is a prominent medical issue and a primary source of death

around the world, in uencing an expected 28.8 million individuals [8] and representing 7.6 million deaths in 2008 [9]. e most frequently analyzed malignancies worldwide are lung (12.7%), breast (10.9%), colorectal (9.7%) and stomach (7.81%), among others (Bray et al.). In recent years, the health impacts of dietary polyphenols have been drawing in the consideration of scientists, nutritionists and nourishment makers. eir strong antitumor properties, richness in the eating regimen, and their sound impacts in the counteractive action of di erent oxidative anxiety related infections, bringing about separate wholesome proposals [10]. Phenolic antioxidants, one of the signi cant category of secondary metabolites, are widely dispersed in the plant kingdom [11]. GA, one of the most signi cant phenolic compounds, is accounted for to treat diverse malignant cell lines [12-16]. GA shows a range of biological actions, and its ester subsidiaries can actuate mitochondrial deterioration. ese subsidiaries are speci cally cytotoxic toward tumor cells [17].

O a, a ca ce,

Ovarian tumor is the second most familiar gynecologic cancer among ladies and the ninth most widespread malignancy in the US [18]. It is one of the main sources of tumor related mortality in ladies in developed countries [19]. In 2015, an expected 21,290 new cases and 14,180 passing because of ovarian malignancy happened in the USA [20]. Unluckily, the general survival rate at 5 years is just 50%, which has not fundamentally enhanced in the previous 30 years [21]. GA has demonstrated the best inhibitory movement on human ovarian malignancy cells among eight characteristic phenolic compounds from conventional Chinese pharmaceutical [22]. It is accounted for to have extraordinary development inhibitory impact on two ovarian disease cell lines, A2780/CP70 and OVCAR-3, than the impact on an ordinary ovarian cell line, IOSE-364. It speci cally suppresses the development of tumor cells and reported to inhibit vascular endothelial growth factor (VEGF) discharge, hence, restrains *in itro* angiogenesis. is polyphenol downregulate AKT phosphorylation in addition to hypoxia-inducible factor-1α (HIF-1α) protein expression, however, enhances PTEN expression. PTEN/AKT/HIF-1α pathway represents the inhibitory impact of GA on *in itro* angiogenesis and VEGF expression [22,23]. *Emblica o cinalis* (Amla) extract, containing GA and its derivatives, does not generate apoptotic cell death, but remarkably increases the expression of the autophagic proteins, LC3B-II and beclin1. It is reported to reduce the expression of several angiogenic genes, including hypoxia-inducible factor 1α (HIF-1α) both in OVCAR3 and SW626 cells [24]. Previous study shows that GA induces anti-ovarian cancer e ects on three ovarian cell lines, OVCAR-8, A2780 and A2780cis [25]. ese discoveries give solid support to the high capability of GA in the anticipation and treatment of ovarian malignancy.

C /c ec a ca ce,

Colon–rectal malignancy is widespread amongst the most well-known malady issues in numerous nations, particularly in the

Previous study demonstrated that Ziyang green tea (ZTP), containing (-) -epigallocatechin gallate (28.2%), followed by (-)-epigallocatechin (5.7%) and (-)- epicatechingallate (12.6%), repress MCF-7 cell multiplication by blocking cell cycle advancement at the G0/G1 stage and triggers apoptotic death. ZTP promotes cell-cycle arrest by upregulation of p53 and down regulation of CDK2 in MCF-7

more and more experiments to con rm these ndings [62,63].

Ga cac da a . - a a e .

In ammation is the leading cause for many chronic health disorders, immune-in ammatory e ect is a protective mechanism to stop the onset of infections caused by wound or microbial invasion. Phenolic compounds are the front line defense of plants like secondary metabolites. e mechanisms of anti-in ammatory e ects of the phenolic compounds are generally considered to arise from their ability of killing free radicals, restoring antioxidant enzyme activities and in regulating cytokine-induced in ammation [71]. GA, naturally occurring polyphenol, exerts potentially medical useful anti-in ammatory e ects mediated through the suppression of p65-NF-κB and IL-6/p-STAT3Y705 activation. In gallic acid anti-in ammatory response, one of the possible given mechanisms involves a reduction of the neutrophilic in ltration in the colon accompanied by a reduced expression of CD68+. Also, the pro-in ammatory proteins iNOS and COX-2 expression reduced by preventing the expressions of p-STAT3Y705 and inhibits the p65-NF-κB-mediated transcriptional activation [72].

C c .

is review presents an attempt to summarize the variable utility of the GA and its derivatives in various forms for di erent therapeutic purposes. e data demonstrate that dietary polyphenol could be a favorable coadjutant agent for disease treatment. To date, GA is evaluated to exhibit substantial and valuable impacts on humans. GA, as polyphenol has emerged as one of the key candidate in the functional food center. Research in the generation and application of this compound is gaining momentum because of diverse medical service and bio-functional properties.

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32. sinense and gallic acid suppress hepatitis C virus infection by blocking early .

33. Antiproliferative and uncoupling effects of delocalized, lipophilic, cationic gallic

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