Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 12 [12] November 2023: 441-449

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

Gallic Acid a Multi-Therapeutic Agent for Pharmaceuticals

Vineeta V. Nagathan1, Kamaladevi Kshatriya1, Hasanpasha N. Sholapur2*, Fatima Sanjeri Dasankoppa1, Revati D. Sagare1, Lakshmi Swapna Sai1
1Department of Pharmaceutics, KLE College of Pharmacy, Hubballi -580 031, India
2Department of Pharmacognosy, KLE College of Pharmacy, Hubballi -580 021, India
Corresponding Author: Dr. Hasanpasha N. Sholapur
Department of Pharmacognosy, KLE College of Pharmacy, Vidyanagar, Hubli-580 031,
Email - hasanpashasholapur@gmail.com

ABSTRACT
Gallic acid (GA) is a naturally occurring polyphenolic compound with many potential medicinal uses in the pharmaceutical industry. Sources of gallic acid, biosynthesis, physical and molecular characteristics, and pharmacokinetic profile are all covered in detail in this review article. The article also covers gallic acid's many pharmacological attributes, such as its anti-inflammatory, anti-cancer, antioxidant, and anti-microbial activities. A detailed exploration of the molecular mechanisms underlying these effects are included along with an overview of the most recent studies on the use of gallic acid for the prevention and treatment of various diseases. The article also includes tables summarising the important discoveries about the antioxidant, anti-cancer, anti-inflammatory and anti-microbial characteristics of gallic acid, as well as a section on the pharmacological profile and formulations of gallic acid. Gallic acid is described in this review article as a promising multi-therapeutic agent having prospective uses in a variety of pharmacological and pharmaceutical sector.
Keywords: *Gallic acid, polyphenol, antioxidant, anticancer anti-inflammatory, antimicrobial.*

Received 23.09.2023 Revised 07.10.2023 Accepted 21.10.2023

INTRODUCTION

Nutraceuticals obtained from plants has played a pivotal role in treatment and maintenance of human disease and health. Food supplements derived from the plant source always contain polyphenols. In the past 20 years, in depth research has been done on how these chemicals affect the human health. The merits of foods obtained from plants have been linked to their metabolites. [1] Chemically known as 3, 4, 5-trihydroxybenzoic acid, GA is a phenolic substance that naturally exists in a number of plants, including *Allan blackia floribunda, Caesalpinia sappan, Dillenia indica, and Psidium guajava, Vitis vinifera, Hamamelis virginiana, Syzygium cordatum, and Toonasinensis Oenothera bienni* with a low molecular weight that has strong anti-inflammatory and antioxidative properties among the various polyphenols.[2,3] Vegetables, grapes, berries, tea and wine are all naturally high in GA, as a phytochemical. Since GA has properties that set it apart from other polyphenols, including a spectrum of time and dose-dependent strategies to exert its effects. GA and its derivatives have additionally proven to be beneficial for tackling and/or inhibiting inflammatory-state conditions like skin inflammation, the healing of injuries, skin infections, arthritis, allergic responses like asthma, allergic rhinitis, and sinusitis, obesity, diabetes, cardiovascular disorders like myocardial dysfunctions linked to type 1 diabetes (T1D), hepatic damage epilepsy and mutagenesis due to their ability to reduce inflammation. Many research has demonstrated that GA is utilised in the pharmaceutical sector to create antibacterial medications (such as trimethoprim) and antifungal delivery methods.[4]Additionally, GA has a number of significant pharmacological effects, such as anti-tumour, anti-microbial and anti-myocardial ischemia.[1]

GALLIC ACID SOURCES, BIOSYNTHESIS AND PROPERTIES

The most widely distributed gallic acid plant sources are *Pueraria lobata* (Wild.) Ohwi, *Guazuma ulmifolia* Lam., *Sambucus nigra* L., *Phyllanthus amarus* Schum. & Thonn, *Mentha spicata* L., *Achillea schischkinii* D.Sosn etc., form these sources gallic acid is extracted by various methods.[2]

Solvent Extraction: The natural source material is macerated or pulverised in the solvent extraction process before being extracted with an organic solvent such ethyl acetate, methanol, or ethanol. The solvent

is subsequently removed from the extract, which is then concentrated and filtered to produce a crude extract. To obtain gallic acid, this crude extract can be further refined using methods like chromatography.
Enzymatic extraction: In this process, the natural source material is broken down and gallic acid is released. For instance, tannins can be hydrolysed to liberate gallic acid using tannase or other hydrolytic enzymes. After filtering the resultant mixture, gallic acid is separated and purified.
Microwave assisted extraction: The natural source material is combined with a solvent and subjected to microwave radiation. The microwaves' heat aids in rupturing the cell walls and releasing the gallic acid into the solvent. After filtering the resultant mixture, gallic acid is separated and purified.
Supercritical fluid extraction: Gallic acid is extracted from the natural source material using a supercritical fluid, such as carbon dioxide, in this process. GA is extracted into the fluid by pumping the fluid through the substance. GA is precipitated out of the solution as the fluid is depressurized. After that, the gallic acid can be gathered and purified.
Solid-phase extraction: In this method, a solid-phase adsorbent like activated charcoal or silica gel is used to selectively absorb gallic acid from a solution. A column filled with adsorbent is used to filter the solution. GA is adsorbed onto the column in contrast to other chemicals, which are washed away. Once the gallic acid has been eluted from the column, it can be purified.[5]
GA and its derivatives, including galloyl glucosides, KMU-3, Tryptamine-GA hybrids and esters, generally known as gallates, can also be synthesised chemically or by microorganisms. [4]
Gallic acid is also produced by hydrolysing tannins with an acid or an enzyme. GA is produced **commercially** by hydrolysing plant-based tannins (Gallo tannins), such as pentagalloylglucose, either through chemical hydrolysis or enzymatic hydrolysis.[6]

BIOSYNTHESIS

Branchpoint reactions from 3-dehydroshikimic acid can result in the formation of gallic acid (3,4,5-trihydroxybenzoic acid), which involves dehydration and enolization or, in the case of gallic acid, dehydrogenation and enolization. [7]
Many tannins, which are plant substances that have been used for thousands of years to tan animal hides and produce leather because of their capacity to cross-link protein molecules, include gallic acid as a component.[7] Figure 1 represents the formation of gallic acid through shikimic acid pathway.

PHYSICAL AND CHEMICAL PROFILE

GA is an organic acid with phenolic and carboxylic acid characteristics that only has one benzene ring structure. Its chemical formula is C7H6O5 and the 3, 4, and 5 positions each have an adjacent OH group. The first position has a COOH group. [9] Table 1 represents the physical and chemical properties of GA, providing a comprehensive overview of its solubility, melting point and other important characteristics.
Numerous investigations have shown that a significant portion of GA is present in the seeds, roots, stems, skins, leaves, flowers and fruits of many medicinal plants, including *Phyllanthus A*. (Euphorbiaceae), *Momordica C*. (Cucurbitaceae), *Achillea S*. (Asteraceae), *Mentha S*. (Lamiaceae) and *Abutilon P*. (Malvaceae).[2]

PHARMACOKINETIC PROPERTIES

If we have a thorough understanding of the pharmacokinetic characteristics of such drugs, we could better comprehend the body's systems for medicine assimilation, dissemination, biotransformation and evacuation i.e., ADME. The following pharmacokinetic properties of GA was thoroughly identified by Yu et al. in Sprague-Dawley rats:.[2] These have been outlined in Table 2.

Toxicity of Gallic Acid

A 210 mg/kg dose of GA had previously been shown to have no harmful effects on BALB/c mice in preclinical study.
This demonstrates that GA is hazardous at dosages that are comparatively higher but remains safe and efficient for a wide range of cells at lower doses. In line with this, GA's in vivo toxicity is minimal.[2]

PHARMACOLOGICAL PROFILE

Antioxidant activity

It is believed that reactive oxygen species play a role in cancer and other disorders.[10,11]
Free radical over production and accumulation lead to oxidative stress, which is the root cause for a number of age-related skin illnesses.[12] Increased production of superoxide radicals and hydrogen peroxide gives rise to oxidative stress. In the presence of a transition metal catalyst, the oxygen-related species can also interact to produce numerous detrimental oxidising species that deplete NADH, GSH and ATP. As a result, these species cause an increase in calcium ions, which damage cells and result in diseases like atherosclerosis, cancer and ischaemia.[11,13] Scavengers of free radicals and antioxidants lessen or delay the production of free radicals and prevent the oxidation of cellular oxidizable substrates. GA has been found to be a strong antioxidant in emulsion or lipid systems, which are frequently employed in food packaging, cosmetics and food preservation.[6] To evaluate the antioxidant activity of gallic acid in various

formulation types, a comprehensive study was conducted, considering different methods of preparation. The results are summarized in Table 3, highlighting the antioxidant activity of GA in each formulation and the corresponding method of preparation.

Anticancer properties

Myeloma cell invasion and migration could be greatly reduced by GA and its derivatives. They have an ability to control the expression of several genes involved in cell cycle, metastasis, angiogenesis and apoptosis, as well as inhibit cancer cells that are using distinct routes. By reducing the activity of anti-apoptotic proteins and boosting the activity of pro-apoptotic proteins, gallic acid causes apoptosis in a variety of cancer cell types. GA, according to Lazaro et al. (2011), generates a large number of topo I and topo II-DNA complexes in cells. Cell death is brought upon by these topoisomerase-DNA complexes, which causes the permanent strand breaks. Additionally, it has been claimed that the gallic acid's pyrogallol moiety also produces these complexes by generation of hydrogen peroxide.[6] To assess the potential anticancer properties of GA, an investigation was conducted involving various cancer types and their respective cell lines treated with gallic acid. The IC50 values, representing the concentration at which gallic acid inhibits 50% of cell growth, were determined, along with the observed effects of GA on cancer cells. A comprehensive summary of these findings is presented in Table 4.

Anti-inflammatory activity

The dynamic process of inflammation is greatly influenced by proinflammatory cytokines such as tumour necrosis factor-alpha, interleukin-1 beta and vascular permeability factor. To combat inflammation, a variety of "Biopharmaceuticals" have evolved, such as drugs that reduce the number of B lymphocytes, which prevent lymphocytes from entering tissues, prevent monocyte-lymphocyte costimulatory molecules from interacting with them, or reduce the activity of particular cytokine-associated receptors (cytokine antagonists).[14]

Mast cells are responsible for initiating and maintaining allergen-triggered inflammation, which are regulated by TNF-α and IL-6. TNF-α is believed to be a primary cytokine that triggers inflammatory processes, leukocyte accumulation, granulomatous inflammation and tissue fibrogenesis, thus contributing to cytokine-related inflammatory conditions. On the other hand, GA has been found to inhibit IgE-mediated and systemic allergy reactions by blocking histamine release and the generation of pro-inflammatory cytokines, ultimately reducing mast cell-triggered allergic inflammation.[15]

In Jurkat -NF-κ-B- RE- bla cells, it was discovered that TC extract inhibited TNF-induced NF-α activation. This was attributed to the inhibition of Iκ-Bα phosphorylation and degradation. It has been noted that I3C can prevent IκBα from degrading and being phosphorylated in a variety of cell types where TNFα has activated NF-κB.[16] The anti-inflammatory activity is presented in Table 5, showcasing the formulation type, method of preparation and corresponding outcomes.

Anti-microbial Activity

Research has revealed that GA has antimicrobial activity against a variety of microorganisms, including Staphylococcus aureus*, Corynobacterium accolans* (human pathogen), *Erwinia carotovora* (plant pathogen) and *Candida albicans* (human pathogenic yeast). [17] In a study on the antimicrobial activity of GA and catechins against microbes on cultures of Helicobacter pylori, researchers used various methods, including colony-forming units, agar disc diffusion assay and measurement of absorbance at 600 nm, to assess the efficacy of the polyphenols. Both GA and catechin demonstrated potent growth inhibitory effects assessed on two H. pylori strains (26695 and ATCC 43504). The extent of antimicrobial action was dependent on the dose, duration and nature of the polyphenolic compound used. GA was found to be more effective than catechin in inhibiting the growth of both H. pylori strains. Additionally, there was proof that GA and catechin had a partially synergistic growth-inhibitory effect. [18] Triphala is an ancient ayurvedic remedy that has been used for centuries in India and is currently being researched as a potential treatment for a number of ailments. The combination of TAE (Triphala hydroalcoholic extract) with other organic antimicrobial substances could potentially enhance the overall antimicrobial activity and effectiveness of the treatment. This approach could be explored as a natural and potentially less harmful alternative to conventional antimicrobial agents.[19]The antimicrobial activity of gallic acid is summarized in Table 6, presenting the formulation type, method of preparation and the corresponding antimicrobial outcomes.

PHARMACEUTICAL PROFILE / FORMULATIONS

GA has been utilised in pharmaceutical formulations in a variety of dosage forms, including tablets, capsules, creams and ointments, due to its medicinal potential and beneficial physicochemical properties. Innovative methods, such as nanoencapsulation, liposomal administration and complexation with cyclodextrins, have been used to address the bioavailability and stability of GA in various pharmaceutical formulations in order to increase its therapeutic potential and ensure optimal drug delivery.

Table 1: Physical and Chemical Properties of Gallic acid. [9]

Tests	Results
Odour	Odourless
State	Crystalline prisms or needles
Colour	Colourless or slightly yellow.
Melting point	432 - 464°C
Log P	Log Ko/w =0.70
Acidic pKa	4.21
LC-MS	Precursor m/z -169
GC-MS	Peak - 170.0 99.99
1H NMR Spectra	Shifts [ppm]: Intensity - 7.03:100.00
13C NMR Spectra	Shifts [ppm]: Intensity - 110.92:1000.00
1H-13C NMR Spectra	Shifts [ppm]: Intensity - 7.04:112.19:1.00
UV Spectra	MAX ABSORPTION (ALC): 272.5 NM (LOG E= 4.06)

Table 2: Pharmacokinetic properties of gallic acid [2]

Parameter	Results
Time of peak plasma level (T max)	1.5 h
Peak plasma concentration (C max)	0.83 µg/mL
Elimination half-life (T1/2)	2.56 h
Cumulative plasma concentration (AUC)	0.137 mg/ min/mL
Mean residence time (MRT)	2.67 h
Clearance rate (CL)	0.37 L/min/kg
Volume distribution (VD).	78.52 L/Kg

Table 3: Anti-oxidant activity of gallic acid containing pharmaceutical formulations

Formulation Type	Method Of Preparation	Results
Gallic acid loaded poloxamer gel [20]	Poloxamer gel was prepared according to the "cold technique"	Studies on the migration of dermal cells and malignant melanoma cells using scratch wound healing and gels laden with gallic acid have demonstrated that these techniques can impede cell migration. This shows that the use of gallic acid as an adjuvant therapy for melanoma treatment is a possibility.
Capsule Dosage Form from Mixed Extracts of Garcinia Mangostana Rind and Solanum Lycopersicum Fruit [21]	By Encapsulation	Capsule dosage form containing mixed extracts of GMR and SLF possesses in vitro antioxidant potential
Tinospora Cordifolia Tablet [22]	By wet Granulation	The study validates the use of a developed Tinospora cordifolia tablet formulation in the management of a wide range of transmissible diseases. The tablet may also be a promising source of bioactive substances, which could reduce oxidative stress and have additional beneficial impacts on health.
Supplementation of gallic acid along with modified pellet diet [23]	GA was administered orally every day for 30 weeks at a weight-based dose of 50 mg/kg body weight after being instantly dissolved in water.	A better protective effect was seen compared to other dietary plans when gallic acid (GA) supplementation was given to rats treated with DMH (dimethylhydrazine) throughout the experimental period. According to the findings, GA serves a purpose in deterring the progression of pre-cancerous lesions into malignant tumours.
Phytoextract Loaded-Pharmaceutical Creams [24]	The preparation of herbal creams may involve the modified methodology using isolated phytochemicals or the extracts along with appropriate composition of the mandatory	The synergistic impact of several ingredients may be attributable to the anti-ageing benefits of cream blends that have been documented. The plant-derived phenolics and flavonoids contained in a variety of natural botanical supplements have been shown to be effective against UVR damage, which is a primary cause of skin ageing.

	constituents essentially employed for creams with desirable features	
Anti-Venom Herbal Paste [25]	The herbal paste was prepared based on a traditional method.	The herbal paste was found to be rich in chemical constituents and exhibited potent in vitro antioxidant activity.
The gel contained elastomeric niosomes that were filled with gallic acid [26]	In the study, gallic acid-loaded niosomes, either as pure compounds or as fractions with partial purification, were produced in both elastic and nonelastic forms.	According to the study, elastic niosomes in particular have the potential to stabilise the chemical properties and enhance the ability of gallic acid to penetrate the skin in the semi-purified fraction derived from T. chebula galls. This research shows that topical anti-ageing products may be more effective when niosomes are included.

Table 4: Anti-cancer properties of gallic acid

Cancer	Type Of Cell Treated With GA	IC50	Effect of Gallic Acid
Colon cancer [27]	HCT116 and HT29 cells	Data not available	cell apoptosis
Cervical cancer [28]	HeLa and HTB-35	80 μM	Apoptosis
Leukemia [29]	(HL-60)	24mM	Apoptosis and antiproliferative
Prostate cancer [30]	DU145	15.6 μg/mL	Apoptosis
Breast cancer [31]	MDA-MB231	10 μg/ml	Apoptosis
Brain tumour [32]	U87	Data not available	Apoptosis
Gastric cancer [33]	AGS	0.01 mM	Anti-metastasis
Lung cancer [34]	A549	100-200 μM	Apoptosis
Osteosarcoma [35]	U-2 OS	Data not available	Anti-metastatic
Fibrosarcoma [31]	HT1080	Data not available	Apoptosis

Table 5: Anti-inflammatory activity of gallic acid containing pharmaceutical formulations

Formulation type	Method of preparation	Results
Cyclodextrin/cellulose hydrogel [36, 37]	Cross-Linking Process	The gel-hydroxypropyl-β-cyclodextrin (HPβ) network appears to have certain characteristics that make it more suited for the inclusion of gallic acid, and this has the potential to be used as an antibacterial wound dressing that does not cause damage to nearby tissue.
Herbal Gels [38]	Incorporation of different concentration of the drug extract into, polyvinyl alcohol (PVA) hydrogels	These findings stimulated the incorporation of extracts in hydrogel formulations as safe and valuable anti-inflammatory gel.
Liposomes for simultaneous delivery of two polyphenols [39]	By film hydration method	The anti-inflammatory effects of polyphenol-liposomes have been demonstrated to be stronger than those of free polyphenols and not cytotoxic to cells.
Oral drug [40]	They come as solid tablets, capsule, chewable tablets or orally disintegrating tablets to be swallowed or sucked -or as a liquid in the form of drops, syrups, or suspensions, which are prepared by either by granulation for tablets and agitation for syrups.	The ADME (absorption, distribution, metabolism, and excretion) properties of the studied substances were discovered to be within the ranges predicted by QikProp for 95% of known oral medicines. The chemicals also comply with Lipinski's rule of five, which denotes good absorption and bioavailability. According to the study, GA esters may be useful for treating stomach inflammation and further exploration could investigate their potential for other medicinal applications, such as anti-tumour effects.
Tablet and capsule formulations [41]	By direct compression.	The study reveals that immediate-release capsules and tablets with high levels of S. kitaibelii extract were developed to satisfy the demand for solid dosage forms that were cost-effective and high in herbal extract content.

Lozenges [42]	Compressed into lozenges.	An important accomplishment that can help produce more precise and potent herbal medicines is the use of NIR spectroscopy and chemometrics to quantify the active principal content in developed medicinal products.
Liniment [43]	Generally, it involves the process of combining medicinal substances with a base of oil, alcohol, or water through various techniques such as heating, maceration and filtration. Burn Liniment, a traditional Chinese medicine formula, contains a combination of five herbal medicines including *Flos Lonicerae, Rhizoma Polygoni Cuspidati, Pericarpium Granati, Terminalia chebula Retz., and Galla Chinensis.*	In rats with burns, burn liniment was found to have strong anti-inflammatory properties. Histological studies showed that BL therapy resulted in a considerable decrease in inflammatory cells, an elevation in fresh granulation tissue, as well as rapid epithelial tissue repair.
Ointment [44]	Depending on the desired features of the finished product, the process for making ointments might vary, but it often entails mixing medicinal ingredients with an oil or wax base using fusion, emulsification, or integration procedures.	The research demonstrated that between three and five hours after giving carrageenan, the ointment reduced paw oedema.

Table 6: Anti-microbial activity of gallic acid containing pharmaceutical formulations

Formulation type	Method of preparation	Results
Nanoemulgel [19]	A nanoemulsion was used in the hydrogel formulation as a lipid-based vector and was disseminated in the gel as a water-based carrier.	In comparison to a traditional cream formulation, the optimised nanoemulgel system formulation, including TAE (Triphala hydroalcoholic extract) -carvacrol, was found to have much stronger antibacterial activity. As a result, it is possible that the nanoemulgel method may perform well for delivering TAE-carvacrol.
Gels [45]	Gels are formulated by incorporating drugs in a semi rigid structure of polymer	A gel with 3.5% gallic acid has been developed and evaluated for its medicinal properties as well as its antibacterial and antifungal efficacy. The in-house punica gel was the most efficient against *Bacillus subtilis, Pseudomonas aeruginosa, Klebsiella pneumonia, and Aspergillus niger*. The gel had high antibacterial and antifungal activity.
Gallic acid liposomes decorated with lactoferrin [46]	A thin-layer dispersion method	The study discovered that in simulated digestion, LF-GA-LIP, a liposome formulation of gallic acid embellished with lactoferrin, exhibited a delayed-release impact in comparison to GA-LIP. LF-GA-LIP also showed higher antibacterial activity against *Escherichia coli and Staphylococcus aureus* compared to GA-LIP. According to these findings, LF-GA-LIP may be useful as a delivery mechanism in the food business.
Gallic acid-coated silver nanoparticles [47]	The method used to prepare nanoparticles will depend on the specific application and the desired properties of the nanoparticles and can involve physical, chemical, or biological methods.	According to the research, GA-AgNPs demonstrated antibacterial efficacy against *Escherichia coli, Staphylococcus aureus, and Candida albicans* with minimum inhibitory concentrations of 6, 30, and 24 g/mL, respectively. Furthermore, the GA was used as both a reducing and stabilising agent, resulting in a straightforward and environmentally friendly preparation process for the GA-AgNPs (Gallic acid-coated silver nanoparticles).
Agar/gelatin microcapsules [48]	Agar was associated with gelatin as the wall matrix material of microcapsules as it could crosslink with gelatin to	The acute liver and kidney damage brought on by an excess of acetaminophen was successfully treated with the gallic acid-loaded microcapsules in an in vivo mouse disease model. They are flexible and due to their effective delivery

	give gel network in the microcapsules formation.	technique these agar-gelatin microcapsules can be applied topically as well as orally.

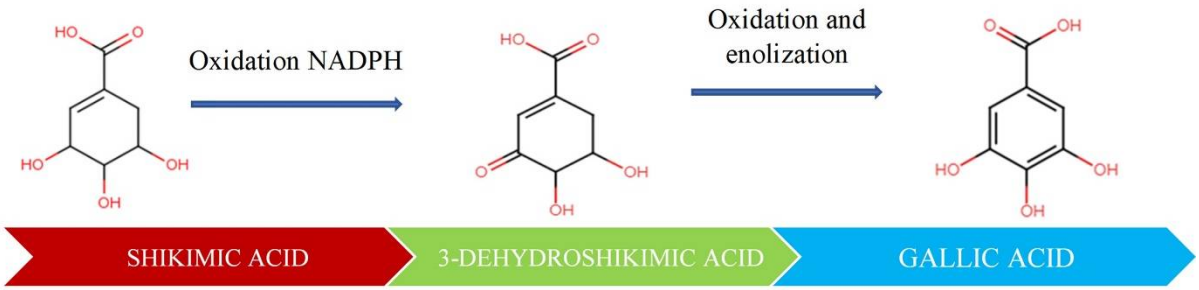

Figure 1: Formation of gallic acid via Shikimic acid pathway. [6,8]

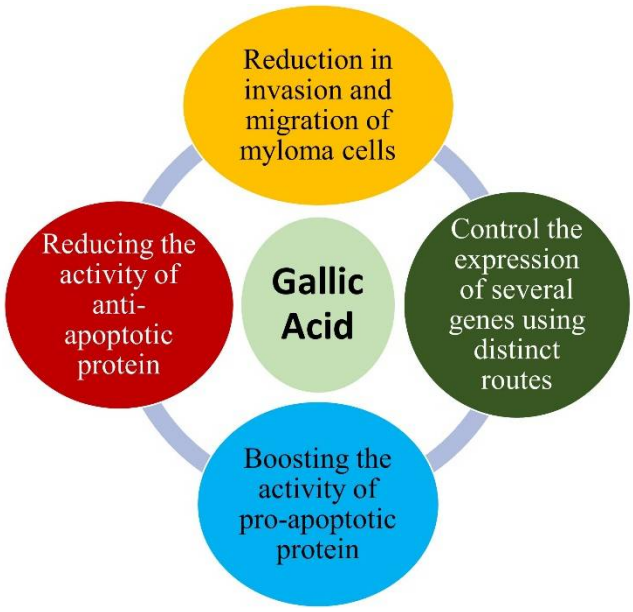

Figure 2: Representing the anticancer activity of gallic acid.

CONCLUSION

In accordance with the present review, information on gallic acid has been thoroughly discussed, covering its sources, biosynthesis, physical and chemical characteristics, and pharmacokinetic profile along with its antioxidant, anticancer anti-inflammatory and antimicrobial activities. GA, a prospective multi-therapeutic agent merits more research and development for usage in a variety of pharmacological domains.GA has shown tremendous potential in pre-clinical and clinical research, despite some limitations, and offers a viable route for the creation of novel medicines and nutraceuticals. To fully achieve its therapeutic commitment, future research should concentrate on optimising its dosage and availability as well as thoroughly comprehending its mechanisms of action.

ACKNOWLEDGEMENT

The authors are thankful to KLE Academy of Higher Education and Research, Belagavi for providing the facilities to compile the review.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

All the authors listed have equally contributed in the preparation of this review.

FUNDING

Preparation of this review was not funded by any agencies.

REFERENCES

1. Badea M, Di Modugno F, Floroian L, Tit DM, Restani P, Bungau S et. al. (2019): Electrochemical strategies for gallic acid detection: Potential for application in clinical, food or environmental analyses. Sci Tot Env 2019;672:129-40.
2. Bai J, Zhang Y, Tang C, Hou Y, Ai X, Chen X et al. (2021): Gallic acid: Pharmacological activities and molecular mechanisms involved in inflammation-related diseases. Biomed pharmacother. 2021;133:110985.
3. Shukla S, Singh B, Singh A, Singh C. (2022): Emerging and Advanced Drug Delivery Systems for Improved Biopharmaceutical Attributes of Gallic Acid: A Review. Phytomed Plus. 2022; 2(4):100369.
4. Khan BA, Mahmood T, Menaa F, Shahzad Y, Yousaf AM, Hussain T et.al. (2018): New perspectives on the efficacy of gallic acid in cosmetics & nanocosmeceuticals. Curr pharm des. 2018;24(43):5181-87.
5. Jahromi SG. (2019): Plant Physiological Aspects of Phenolic Compounds [Internet]. IntechOpen; 2019. Chapter 1, Extraction techniques of phenolic compounds from plants; p.1-8.
6. Choubey S, Goyal S, Varughese LR, Kumar V, Sharma AK, Beniwal V.(2018): Probing Gallic Acid for Its Broad Spectrum Applications. Mini Rev Med Chem 2018;18(15):1283–93.
7. Dewick PM. (2009): Medicinal natural products: a biosynthetic approach. 3rd ed. New York: John Wiley & Sons, Ltd; 2009.
8. Kougan GB, Tabopda T, Kuete V, Verpoorte R. (2013): Medicinal Plant Research in Africa. Elsevier; 2013. Chapter 6, Simple Phenols, Phenolic Acids, and Related Esters from the Medicinal Plants of Africa; p. 225–49.
9. National Center for Biotechnology Information. PubChem Compound Summary for CID 370, Gallic Acid. [Internet] 2023 [updated 2023; cited 2023 May 13]; Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Gallic-Acid.
10. Hu JJ, Dubin N, Kurland D, Ma BL, Roush GC.(1995): The effects of hydrogen peroxide on DNA repair activities. Mutat Res 1995; 336(2):193-201.
11. Yen GC, Duh PD, Tsai HL. (2002): Antioxidant and pro-oxidant properties of ascorbic acid and gallic acid. Food chem 2002; 79(3): 307-13.
12. Monteiro E Silva SA, Calixto GMF, Cajado J, De Carvalho PCA, Rodero CF, Chorilli M, et al. (2017): Gallic acid-loaded gel formulation combats skin oxidative stress: development, characterization and ex vivo biological assays. Polymers (Basel) 2017;9(9): 391.
13. Smith C, Halliwell B, Aruoma OI.(1992): Protection by albumin against the pro-oxidant actions of phenolic dietary components. Food Chem Toxicol 1992; 30(6): 483-9.
14. Dinarello CA. (2010): Anti-inflammatory agents: Present and future. Cell 2010; 140(6): 935-50.
15. Kim SH, Jun CD, Suk K, Choi BJ, Lim H, Park S, et al. (2006): Gallic acid inhibits histamine release and pro-inflammatory cytokine production in mast cells. Toxicol Sci 2006; 91(1): 123–31.
16. Das ND, Jung KH, Park JH, Mondol AM, Shin HJ, Lee HS, et al. (2011): *Terminalia chebula* Extract Acts as a Potential NF-κB Inhibitor in Human Lymphoblastic T Cells. Phytother Res 2011; 25(6): 927–34.
17. Karamac M, Kosińska A, Pegg RB. (2006): Content of gallic acid in selected plant extracts. Pol. J. Food Nutr. Sci 2006; 56(1):55–58.
18. Díaz-Gómez R, López-Solís R, Obreque-Slier E, Toledo-Araya H.(2013): Comparative antibacterial effect of gallic acid and catechin against Helicobacter pylori. LWT-Food Sci Tec 2013;54(2):331–35.
19. Omran Z, Bader A, Porta A, Vandamme T, Anton N, Alehaideb Z, et al. (2020): Evaluation of Antimicrobial Activity of Triphala Constituents and Nanoformulation. Evid Based Complement Alternat Med 2020;2020:11.
20. Sguizzato M, Valacchi G, Pecorelli A, Boldrini P, Simelière F, Huang N, et al. (2020): Gallic acid loaded poloxamer gel as new adjuvant strategy for melanoma: A preliminary study. Colloids Surf B Biointerfaces 2020;185.
21. Azam M, Eden WT, Fibriana AI, Rahayu SR. (2021): Antioxidant properties of capsule dosage form from mixed extracts of *Garcinia mangostana* rind and *Solanum* lycoperIsicum fruit. Acta Pharmaceutica Sciencia 2021;59(1):69–80.
22. Mehra R, Naved T, Arora M, Madan S.(2013): Standardization and evaluation of formulation parameters of Tinospora cordifolia tablet. J Adv Pharm Educ Res 2013;3(4): 440-49.
23. Giftson JS, Jayanthi S, Nalini N.(2010): Chemopreventive efficacy of gallic acid, an antioxidant and anticarcinogenic polyphenol, against 1,2-dimethyl hydrazine induced rat colon carcinogenesis. Invest New Drugs 2010;28(3):251–59.
24. Jadoon S, Karim S, Bin Asad MH, Akram MR, Khan AK, Malik A, et al. (2015): Anti-aging potential of phytoextract loaded-pharmaceutical creams for human skin cell longetivity. Oxid Med Cell Longev 2015; 2015:709628.
25. Kulatunga WMSSK, Arawwawala LDAM. (2021): Chemical Analysis of Anti-Venom Herbal Paste Use in Sri Lanka. South Asian Res J Nat Prod 2021; 4(4): 1-7.
26. Manosroi A, Jantrawut P, Akazawa H, Akihisa T, Manosroi W, Manosroi J. (2011): Transdermal absorption enhancement of gel containing elastic niosomes loaded with gallic acid from Terminalia chebula galls. Pharm Biol 2011;49(6):553–62.
27. Lin X, Wang G, Liu P, Han L, Wang T, Chen K, et al. (2021): Gallic acid suppresses colon cancer proliferation by inhibiting SRC and EGFR phosphorylation. Exp Ther Med 2021;21(6): 638.
28. You BR, Moon HJ, Han YH, Park WH. (2010): Gallic acid inhibits the growth of HeLa cervical cancer cells via apoptosis and/or necrosis. Food Chem Toxicol 2010;48(5):1334–40.

29. Huang PJ, Hseu YC, Lee MS, Senthil Kumar KJ, Wu CR, Hsu LS, et al. (2012): In vitro and in vivo activity of gallic acid and Toona sinensis leaf extracts against HL-60 human premyelocytic leukemia. Food Chem Toxicol 2012;50(10):3489–97.
30. Chen HM, Wu YC, Chia YC, Chang FR, Hsu HK, Hsieh YC, et al. (2009): Gallic acid, a major component of Toona sinensis leaf extracts, contains a ROS-mediated anti-cancer activity in human prostate cancer cells. Cancer Lett 2009;286(2):161–71.
31. García-Rivera D, Delgado R, Bougarne N, Haegeman G, Vanden Berghe W. (2011): Gallic acid indanone and mangiferin xanthone are strong determinants of immunosuppressive anti-tumour effects of Mangifera indica L. bark in MDA-MB231 breast cancer cells. Cancer Lett 2011;305(1):21–31.
32. Lu Y, Jiang F, Jiang H, Wu K, Zheng X, Cai Y, et al. (2010): Gallic acid suppresses cell viability, proliferation, invasion and angiogenesis in human glioma cells. Eur J Pharmacol 2010;641(2–3):102–7.
33. Ho HH, Chang C Sen, Ho WC, Liao SY, Wu CH, Wang CJ. (2010): Anti-metastasis effects of gallic acid on gastric cancer cells involves inhibition of NF-κB activity and downregulation of PI3K/AKT/small GTPase signals. Food Chem Toxicol 2010;48(8–9):2508–16.
34. You BR, Park WH. (2010): Gallic acid-induced lung cancer cell death is related to glutathione depletion as well as reactive oxygen species increase. Toxicology in Vitro 2010;24(5):1356–62.
35. Arndt CA, Rose PS, Folpe AL, Laack NN. (2012): Common musculoskeletal tumors of childhood and adolescence. Mayo Clin Proc 2012; 87(5):475-87.
36. Pinho E, Henriques M, Soares G. (2014): Cyclodextrin/cellulose hydrogel with gallic acid to prevent wound infection. Cellulose 2014; 21:4519-30.
37. Rodriguez-Tenreiro C, Alvarez-Lorenzo C, Rodriguez-Perez A, Concheiro A, Torres-Labandeira JJ. (2006): New cyclodextrin hydrogels cross-linked with diglycidylethers with a high drug loading and controlled release ability. Pharm Res 2006; 23(1): 121–30.
38. Yousif MF, Haider M, Sleem AA. (2011): Formulation and Evaluation of Two Anti-inflammatory Herbal Gels. J Biol Act Prod Nat 2011;1(3):200–9.
39. Giordani B, Basnet P, Mishchenko E, Luppi B, Škalko-Basnet N. (2019): Utilizing liposomal quercetin and gallic acid in localized treatment of vaginal Candida infections. Pharmaceutics 2019; 12(1):9.
40. Dhingra MS, Dhingra S, Chadha R, Singh T, Karan M. (2014): Design, synthesis, physicochemical, and pharmacological evaluation of gallic acid esters as non-ulcerogenic and gastroprotective anti-inflammatory agents. Med Chem Res 2014;23(11):4771–88.
41. Mudrić J, Arsenijević J, Maksimović Z, Ibrić S, Gopčević K, Đuriš J. (2021): Tablet and capsule formulations incorporating high doses of a dry optimized herbal extract: The case of Satureja kitaibelii. J Drug Deliv Sci Technol 2021; 66: 102776.
42. Gavan A, Toiu AM, Tamaș M, Tomuță I. (2017): Dry rose petal extracts and compressed lozenges: formulation and NIR–Chemometric quantification of active principles. Farmacia 2017; 65(4):577-83.
43. Wang X, Zhao QS, Zhao CL, Guo H, Peng SW, Wu JH. (2014): Effect of Chinese medical herbs-burn liniment on deep second degree burn in rats. Afr J Tradit Complement Altern Med 2014;11(6):92-104.
44. Pergolizzi S, D'Angelo V, Aragona M, Dugo P, Cacciola F, Capillo G, et al. (2020): Evaluation of antioxidant and anti-inflammatory activity of green coffee beans methanolic extract in rat skin. Nat Prod Res 2020;34(11):1535–41.
45. Chalke T, Sharma K, Nagare SK, Jirge SS. (2016): Formulation and evaluation of punica topical gel for its content of gallic acid and anti-microbial study. Int J Drug Deliv Technol 2016;6(3):75-78.
46. Zhang Y, Pu C, Tang W, Wang S, Sun Q. (2019): Gallic acid liposomes decorated with lactoferrin: Characterization, in vitro digestion and antibacterial activity. Food Chem;293:315–22.
47. Li D, Liu Z, Yuan Y, Liu Y, Niu F. (2015): Green synthesis of gallic acid-coated silver nanoparticles with high antimicrobial activity and low cytotoxicity to normal cells. Process Biochem;50(3):357–66.
48. Lam PL, Lee KKH, Kok SHL, Cheng GYM, Tao XM, Hau DKP, et al. (2012): Development of formaldehyde-free agar/gelatin microcapsules containing berberine HCl and gallic acid and their topical and oral applications. Soft Matter;8(18):5027–37.

CITATION OF THIS ARTICLE

Vineeta V. Nagathan1, Kamaladevi Kshatriya1, Hasanpasha N. Sholapur2*, Fatima Sanjeri Dasankoppa1, Revati D. Sagare1, Lakshmi Swapna Sai1.Gallic Acid a Multi-Therapeutic Agent For Pharmaceuticals. Bull. Env.Pharmacol. Life Sci., Vol 12 [12] November 2023: 441-449