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PHARMACOLOGICAL POTENTIAL OF LUTEOLIN-7-O-GLUCOSIDE: MOLECULAR MECHANISMS UNDERLYING ITS ANTICANCER, ANTI-INFLAMMATORY, AND NEUROPROTECTIVE ACTIVITIES

[1*]Dr. Arti S. Dange, [2]Dr. Ashwin A. Shete, [3]Hrushikesh S. Dange

Dr. Dy Patil College of Ayurveda and Research Centre Pimpri, Pune 411017, Maharashtra, India.

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***Corresponding Author**

Dr. Arti S. Dange

Dr. Dy Patil College of Ayurveda and Research Centre Pimpri, Pune 411017, Maharashtra, India.

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ABSTRACT

Luteolin-7-O-glucoside (LUT-7G), also known as cynaroside, is a naturally occurring flavonoid glycoside widely distributed in medicinal plants and dietary sources. Growing evidence has highlighted its diverse pharmacological activities, including anticancer, anti-inflammatory, antioxidant, antimicrobial, and neuroprotective properties. The therapeutic potential of LUT-7G is primarily attributed to its ability to regulate multiple intracellular signaling pathways involved in cell proliferation, apoptosis, oxidative stress, inflammation, and metabolic reprogramming. In cancer, LUT-7G suppresses tumor progression through induction of apoptosis, inhibition of epithelial-mesenchymal transition (EMT), modulation of the Warburg effect, and regulation of JAK/STAT, PI3K/Akt, ERK, Wnt/β-catenin, and Notch signaling pathways. Furthermore, LUT-7G demonstrates potent anti-inflammatory activity by suppressing NF-κB, IL-22/STAT3, and JAK1/STAT6 signaling while reducing the production of pro-inflammatory cytokines. Recent studies have also reported significant neuroprotective effects against Alzheimer's disease and Parkinson's disease through attenuation of oxidative stress, inhibition of amyloid-β aggregation, suppression of neuroinflammation, and prevention of neuronal apoptosis. This review summarizes the current evidence regarding the pharmacological activities, molecular mechanisms, and therapeutic potential of LUT-7G

while highlighting existing research gaps and future clinical prospects.

KEYWORDS: Luteolin-7-O-glucoside; Cynaroside; Flavonoids; Cancer; Inflammation; Neuroprotection; JAK/STAT; Wnt/β-catenin; Oxidative stress.

INTRODUCTION

Natural products have long served as an important source of therapeutic agents owing to their structural diversity and broad biological activities.[1,2] Among these compounds, flavonoids constitute one of the largest classes of polyphenolic metabolites and exhibit antioxidant, anti-inflammatory, anticancer, antimicrobial, antiviral, and neuroprotective properties.[3-5] Luteolin-7-O-glucoside (LUT-7G), commonly known as cynaroside, is a glycosylated derivative of luteolin that occurs naturally in several medicinal plants, including *Lonicera japonica*, *Cuminum cyminum*, *Ophiorrhiza* species, *Chrysanthemum morifolium*, and *Taraxacum officinalev.*[6,7]

Recent pharmacological investigations have identified LUT-7G as a promising bioactive molecule with the ability to regulate multiple molecular targets involved in chronic diseases. Unlike conventional drugs that typically affect a single target, LUT-7G acts on several signaling pathways simultaneously, thereby producing pleiotropic therapeutic effects.[8] Experimental evidence demonstrates that LUT-7G induces apoptosis, inhibits angiogenesis, suppresses epithelial-mesenchymal transition (EMT), and interferes with metabolic reprogramming in various cancer cell lines. In addition, it effectively modulates inflammatory mediators by inhibiting NF-κB, JAK/STAT, PI3K/Akt, and MAPK signaling pathways while reducing oxidative stress through enhancement of endogenous antioxidant defense systems.[7-8] These mechanisms collectively contribute to its therapeutic efficacy against cancer, inflammatory disorders, and neurodegenerative diseases.

Despite substantial progress in understanding its biological activities, the molecular mechanisms and translational potential of LUT-7G remain incompletely characterized. Therefore, a comprehensive review of the available evidence is essential to facilitate future pharmacological and clinical investigations.[9]

To comprehensively review the pharmacological activities, molecular mechanisms, and therapeutic potential of luteolin-7-O-glucoside in the prevention and management of cancer, inflammatory diseases, and neurodegenerative disorders.

Literature Search Methodology

A systematic literature search was performed using electronic databases including PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. Publications from 2005 to 2025 were searched using the keywords *Luteolin-7-O-glucoside*, *Cynaroside*, *Flavonoids*, *Cancer*, *Anti-inflammatory*, *Neuroprotection*, *Oxidative stress*, *JAK/STAT*, *EMT*, *Wnt/β-catenin*, and *Alzheimer's disease*. Original research articles, review articles, and experimental studies published in peer-reviewed English-language journals were included. Conference abstracts, duplicate records, editorials, and studies lacking adequate experimental evidence were excluded. Preference was given to articles indexed in Scopus and Web of Science.[5,9]

Table 1. Natural Sources of Luteolin-7-O-Glucoside (LUT-7G)

Plant source	Family	Plant part	Major phytoconstituent	Reported pharmaological activity
Lonicera japonica (Japanese honeysuckle)	Caprifoliaceae	Flowers	Luteolin-7-O-glucoside	Anti-inflammatory, antioxidant
Chrysanthemum morifolium	Asteraceae	Flowers	LUT-7G	Neuroprotective, antioxidant
Cynara scolymus (Artichoke)	Asteraceae	Leaves	Cynaroside	Hepatoprotective, antioxidant
Cuminum cyminum (Cumin)	Apiaceae	Seeds	LUT-7G	Anticancer, antimicrobial
Ophiorrhiza mungos	Rubiaceae	Whole plant	LUT-7G	Anticancer
Taraxacum officinale (Dandelion)	Asteraceae	Leaves	LUT-7G	Anti-inflammatory
Perilla frutescens	Lamiaceae	Leaves	LUT-7G	Antioxidant
Mentha piperita (Peppermint)	Lamiaceae	Leaves	LUT-7G	Antioxidant
Rosmarinus officinalis (Rosemary)	Lamiaceae	Leaves	LUT-7G	Anti-inflammatory
Thymus vulgaris (Thyme)	Lamiaceae	Leaves	LUT-7G	Antioxidant

Anticancer Activity of Luteolin-7-O-Glucoside

Luteolin-7-O-glucoside (LUT-7G), also known as cynaroside, is a naturally occurring flavonoid that exhibits significant anticancer activity against various malignancies, including breast cancer, oral squamous cell carcinoma, and hepatocellular carcinoma.[2,3] It suppresses tumor growth by inducing apoptosis through activation of the mitochondrial pathway, regulating the Bax/Bcl-2 ratio, and activating caspases. LUT-7G also inhibits cancer cell proliferation by inducing cell-cycle arrest through modulation of cyclins and cyclin-dependent kinases. Furthermore, it suppresses epithelial-mesenchymal transition (EMT) by

downregulating Notch-1, β-catenin, and matrix metalloproteinase-2 (MMP-2), thereby reducing cancer cell migration and invasion.[4] Additionally, LUT-7G interferes with the Warburg effect by inhibiting glucose transporters (GLUT-1/GLUT-4), lactate dehydrogenase A (LDHA), and hypoxia-inducible factor-1α (HIF-1α), leading to impaired tumor metabolism. It also modulates key oncogenic signaling pathways, including JAK/STAT, PI3K/Akt, ERK, and Wnt/β-catenin, resulting in reduced proliferation, angiogenesis, and metastasis.[8] These multitargeted mechanisms highlight LUT-7G as a promising phytochemical for cancer prevention and therapy; however, further preclinical and clinical studies are required to establish its therapeutic efficacy.[11]

Anti-inflammatory Activity of Luteolin-7-O-Glucoside

Luteolin-7-O-glucoside (LUT-7G) exhibits potent anti-inflammatory activity by regulating multiple inflammatory signaling pathways.[1] It inhibits NF-κB activation, thereby suppressing the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, as well as inflammatory mediators including COX-2 and iNOS. In LPS-stimulated RAW264.7 macrophages, LUT-7G attenuates inflammation through modulation of the NF-κB and PI3K/Akt pathways while reducing oxidative stress. It also suppresses the IL-22/STAT3 pathway to alleviate keratinocyte proliferation in psoriasis and regulates the JAK1/STAT6/SOCS1 signaling pathway to reduce intestinal inflammation and promote mucosal healing in ulcerative colitis.[6,7] These findings highlight LUT-7G as a promising natural anti-inflammatory agent for the management of chronic inflammatory diseases.

Neuroprotective Activity of Luteolin-7-O-Glucoside

Luteolin-7-O-glucoside (LUT-7G) exhibits promising neuroprotective effects against neurodegenerative disorders, particularly Alzheimer's disease (AD) and Parkinson's disease (PD), through its antioxidant, anti-inflammatory, and anti-apoptotic properties. It inhibits amyloid-β (Aβ) aggregation and β-secretase (BACE1) activity while suppressing acetylcholinesterase (AChE), thereby improving cholinergic neurotransmission in AD.[7,10] In addition, LUT-7G reduces oxidative stress and neuroinflammation by scavenging reactive oxygen species (ROS) and inhibiting microglial activation. In Parkinson's disease models, LUT-7G enhances the expression of brain-derived neurotrophic factor (BDNF) and glial cell-derived neurotrophic factor (GDNF), promoting dopaminergic neuronal survival and reducing neuronal apoptosis.[12] These multitarget neuroprotective mechanisms suggest that LUT-7G is a promising phytochemical for the prevention and management of

neurodegenerative diseases.

Molecular Signaling Pathways

Luteolin-7-O-glucoside (LUT-7G) regulates multiple signaling pathways involved in cancer, inflammation, and neurodegeneration.[2,3] It inhibits the JAK/STAT, PI3K/Akt, NF-κB, MAPK/ERK, Wnt/β-catenin, and Notch pathways, thereby suppressing cell proliferation, epithelial-mesenchymal transition (EMT), migration, invasion, and inflammatory cytokine production. LUT-7G also disrupts the Warburg effect by downregulating GLUT-1, GLUT-4, LDHA, HK2, and HIF-1α, leading to impaired tumor metabolism. Furthermore, its antioxidant activity reduces reactive oxygen species (ROS) and oxidative stress, contributing to its anticancer, anti-inflammatory, and neuroprotective effects.[7,8,10]

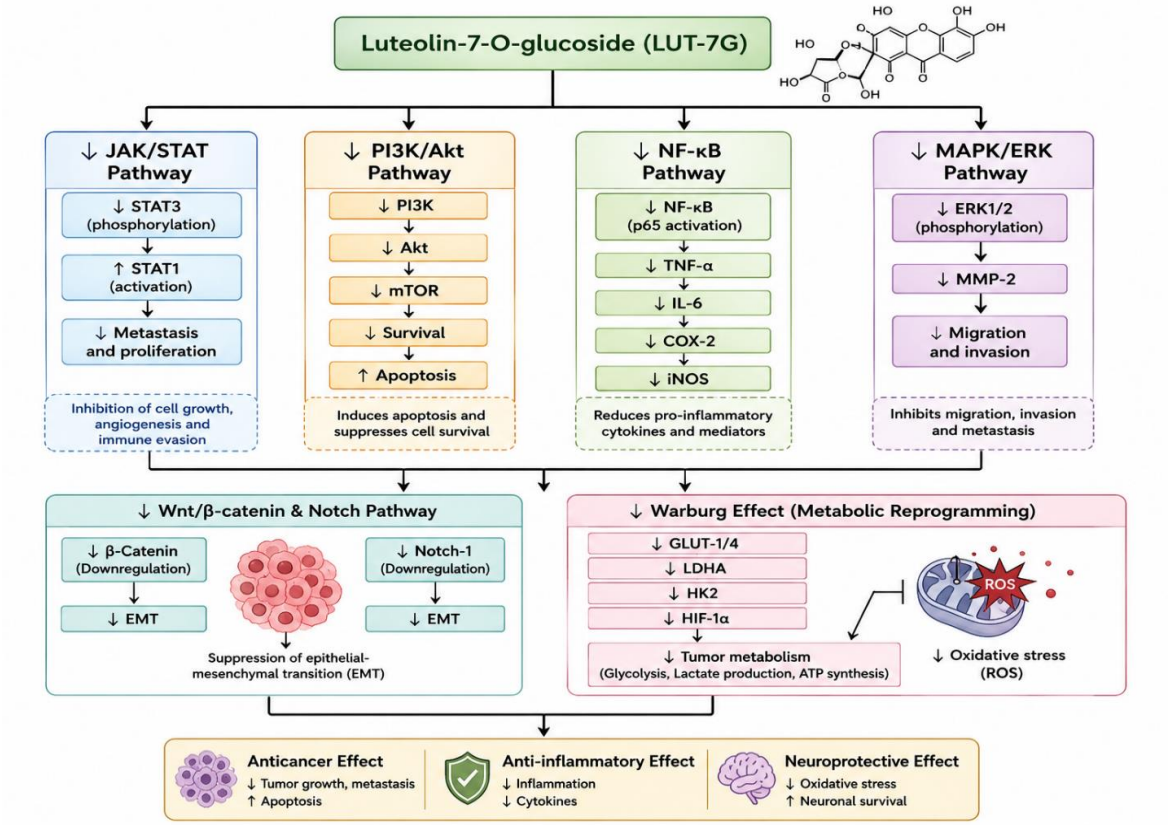

Figure 1: Molecular Signaling Pathways Luteolin-7-O-glucoside (LUT-7G).

Table 2. Molecular Targets and Signaling Pathways Modulated by Luteolin-7-O-Glucoside (LUT-7G)

Molecular target	Signaling pathway	Biological effect	Disease relevance
STAT1	JAK/STAT	↑ Tumor suppressor signaling	Cancer
STAT3	JAK/STAT	↓ Cell proliferation and metastasis	Cancer, inflammation
NF-κB	NF-κB pathway	↓ TNF-α, IL-6, IL-1β	Chronic inflammation
PI3K/Akt	PI3K/Akt	↓ Cell survival	Cancer
ERK1/2	MAPK/ERK	↓ Cell migration	Oral cancer
β-Catenin	Wnt/β-catenin	↓ EMT	Cancer metastasis
Notch-1	Notch pathway	↓ EMT	Cancer
MMP-2	ERK/MMP pathway	↓ Invasion and migration	Oral carcinoma
LDHA	Warburg effect	↓ Glycolysis	Cancer metabolism
GLUT-1	Glucose metabolism	↓ Glucose uptake	Cancer
GLUT-4	Glucose metabolism	↓ Aerobic glycolysis	Cancer
HIF-1α	Hypoxia pathway	↓ Tumor adaptation	Solid tumors
COX-2	Inflammatory pathway	↓ Prostaglandin synthesis	Inflammation
iNOS	Nitric oxide pathway	↓ NO production	Inflammation
IL-22	IL-22/STAT3	↓ Keratinocyte proliferation	Psoriasis
SOCS1	JAK1/STAT6	↑ Anti-inflammatory response	Ulcerative colitis
Aβ peptide	Amyloid pathway	↓ Plaque formation	Alzheimer's disease
BDNF	Neurotrophic pathway	↑ Neuronal survival	Parkinson's disease
GDNF	Neurotrophic pathway	↑ Dopaminergic neuron protection	Parkinson's disease

Table 3. Preclinical Studies and Experimental Models Demonstrating the Biological Activities of Luteolin-7-O-Glucoside (LUT-7G)

Study model	Experimental model	Major findings	Proposed mechanism
RAW264.7 macrophages	LPS-induced inflammation	Reduced TNF-α, IL-6, IL-1β	NF-κB inhibition
Oral squamous carcinoma	SCC cells	Reduced migration	ERK/MMP-2 inhibition
Breast cancer	MCF-7, MDA-MB-231	Apoptosis, cell-cycle arrest	Caspase activation
Hepatocellular carcinoma	HepG2	Reduced proliferation	JAK/STAT inhibition
Psoriasis	Mouse model	Reduced epidermal hyperplasia	IL-22/STAT3 inhibition
Ulcerative colitis	DSS-induced mice	Improved colonic inflammation	JAK1/STAT6/SOCS1 modulation
Alzheimer's disease	Aβ-induced neuronal model	Reduced amyloid toxicity	Antioxidant and anti-apoptotic activity
Parkinson's disease	MPTP mouse model	Improved motor function	Increased BDNF and GDNF
Oxidative stress	H_2O_2-induced cells	Reduced ROS	Antioxidant activity
Antimicrobial assays	Various microorganisms	Growth inhibition	Membrane disruption and oxidative stress

DISCUSSION

The available evidence indicates that luteolin-7-O-glucoside (LUT-7G) is a promising multifunctional flavonoid with significant anticancer, anti-inflammatory, and neuroprotective

potential.[2] Its pharmacological activities are primarily mediated through modulation of multiple signaling pathways, including JAK/STAT, PI3K/Akt, NF-κB, MAPK/ERK, Wnt/β-catenin, and Notch, which collectively regulate apoptosis, inflammation, oxidative stress, epithelial-mesenchymal transition (EMT), and cellular metabolism. Furthermore, inhibition of the Warburg effect and reduction of reactive oxygen species (ROS) contribute to its ability to suppress tumor progression and protect neuronal cells.[3] Preclinical studies have consistently demonstrated that LUT-7G inhibits cancer cell proliferation, attenuates inflammatory responses, and reduces neurodegeneration through its antioxidant and anti-apoptotic properties.[7-8] However, despite these encouraging findings, the majority of available evidence is derived from in vitro and animal studies. Limited information regarding its pharmacokinetics, bioavailability, safety, and long-term efficacy in humans remains a major challenge. Therefore, further well-designed preclinical investigations and randomized clinical trials are necessary to validate the therapeutic potential of LUT-7G and facilitate its clinical translation.[10]

Future Perspectives

Future research should focus on improving the bioavailability of LUT-7G through advanced drug delivery systems such as nanoparticles, liposomes, and phytosomes. Omics-based approaches, molecular docking, and network pharmacology may provide deeper insights into its mechanisms of action. Furthermore, well-designed multicenter clinical trials are required to validate its efficacy and safety in humans and to explore its potential as an adjunct to existing therapeutic regimens.

CONCLUSION

Luteolin-7-O-glucoside is a multifunctional flavonoid with considerable pharmacological potential. Current evidence indicates that it exerts anticancer, anti-inflammatory, antioxidant, and neuroprotective effects by regulating multiple signaling pathways involved in apoptosis, oxidative stress, inflammation, epithelial-mesenchymal transition, and cellular metabolism. Although preclinical data are highly encouraging, further pharmacokinetic investigations and large-scale clinical studies are necessary to establish its therapeutic efficacy and safety. Continued research into LUT-7G may facilitate the development of novel phytopharmaceutical interventions for chronic and complex diseases.

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