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Review Article

Biochemistry of Traditional Herbal Compounds and their Molecular Targets

Anih David Chinonso*, Arowora Adebisi Kayode, Moses Abah Adondua, Ugwuoke Kenneth Chinekwu

Department of Biochemistry, Faculty of Biosciences, Federal University Wukari, Taraba, NIGERIA.

ABSTRACT

Traditional herbal medicine represents a rich and diverse pharmacological reservoir that has long been utilized for treating various ailments across cultures. The growing interest in evidence-based phytotherapy has prompted rigorous scientific investigation into the biochemical and molecular underpinnings of many traditional herbal compounds. This review explores the biochemical nature, mechanisms of action, and molecular targets of five key phytochemicals: plumbagin, β-eudesmol, garcihombronane D, neferine, and iriflophenone 3-C-β-D-glucoside. A detailed analysis of their chemical structures, signaling pathways, and cellular effects is provided, contextualized with recent empirical findings. These compounds exhibit potent anti-inflammatory, anticancer, antioxidant, cardioprotective, and neuroprotective effects by modulating critical signaling pathways, including NF-κB, PI3K/Akt, MAPK, STAT3, and mTOR. Mechanistic insights reveal their roles in regulating apoptosis, autophagy, oxidative stress responses, and angiogenesis, with potential applications in treating chronic diseases. Integrating traditional knowledge with molecular biochemistry underscores the relevance of these natural products as promising candidates for modern drug development. Further preclinical and clinical investigations are needed to optimize their therapeutic application, pharmacokinetics, and bioavailability.

Keywords: Traditional Medicine, Phytochemicals, Molecular Targets, Herbal Compounds, Apoptosis, Natural Products.

Correspondence:
Dr. Anih David Chinonso
Department of Biochemistry, Faculty of Biosciences, Federal University Wukari, Taraba-670102, NIGERIA.
Email: anih.david@fuwukari.edu.ng

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INTRODUCTION

Traditional herbal medicine has formed the foundation of therapeutic systems for centuries, particularly in regions such as Asia, Africa, and Latin America, where medicinal plants are deeply embedded in cultural and healing practices.[2,5] These botanical remedies, rich in phytochemicals, have been historically used to manage a wide range of ailments, though often without detailed understanding of their biochemical or molecular mechanisms.[1,2] The recent shift toward evidence-based validation of traditional medicine has sparked growing scientific interest in exploring the pharmacological potential of herbal compounds, especially as chronic diseases continue to pose significant global health challenges.[3,4] With the limitations of synthetic drugs-such as resistance, side effects, and high development costs-natural products have reemerged as promising candidates for drug discovery due to their structural diversity and biological relevance.[1,4,5]

Recent studies have highlighted the efficacy of several plant-derived molecules in modulating critical cellular processes such as apoptosis, oxidative stress response, and inflammatory signaling. For instance, plumbagin, a naphthoquinone from *Plumbago zeylanica*, has demonstrated the capacity to induce mitochondrial-mediated apoptosis and inhibit the PI3K/Akt/mTOR pathway, thus exerting potent anti-cancer effects *in vitro* and *in vivo* models of melanoma and leukemia.[6,9-11] Similarly, β-eudesmol, isolated from *Atractylodes lancea*, has shown antitumor and anti-angiogenic activity through modulation of ion channels and inhibition of VEGFR2 and PI3K/Akt signaling.[12,14,15] Compounds such as garcihombronane, derived from Garcinia species, are gaining attention for their dual anti-inflammatory and antioxidant actions via STAT3 and Nrf2/HO-1 pathways.[16,20] Moreover, the bisbenzylisoquinoline alkaloid neferine, from *Nelumbo nucifera*, exhibits a range of biological activities including cardioprotective and neuroprotective effects, primarily through AMPK activation and mTOR inhibition.[21-24] Iriflophenone 3-C-β-D-glucoside, a flavonoid glycoside found in Garcinia species, contributes to wound healing and vascular repair by enhancing VEGF expression and collagen biosynthesis through TGF-β signaling.[28-31]

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The structure-activity relationships of these phytochemicals have been further elucidated through advancements in molecular docking, omics technologies, and bioinformatics, providing insights into their interactions with specific proteins, enzymes, and transcription factors.[1,4,5] Reviews have also underscored the pharmacological relevance of natural products in modulating complex signaling networks implicated in oncogenesis, inflammation, and metabolic syndromes.[2,3] Despite these promising findings, challenges such as poor solubility, bioavailability, and lack of clinical validation remain significant obstacles to their therapeutic deployment.[49,50]

This study aims to explore the biochemical characteristics and molecular mechanisms of five key traditional herbal compounds-plumbagin, β-eudesmol, garcihombronane D, neferine, and iriflophenone 3-C-β-D-glucoside. By integrating existing empirical data and mechanistic insights, we assess their pharmacological potential and translational relevance in the treatment of chronic diseases. This article seeks to advance current knowledge by offering a comparative biochemical analysis of these compounds, highlighting their shared and unique molecular targets, and identifying prospects for future therapeutic development.

MOLECULAR BIOCHEMISTRY OF SELECTED HERBAL COMPOUNDS

Plumbagin

Plumbagin is a naturally occurring naphthoquinone isolated from *Plumbago zeylanica*. It is lipophilic and characterized by a quinonoid moiety that facilitates redox cycling, generation of Reactive Oxygen Species (ROS), and inhibition of key signaling proteins.[6] The chemical structure shown in Figure 1 reveals a 1,4-naphthoquinone core, which underpins plumbagin's redox activity. This moiety is crucial for its ability to undergo redox cycling and generate ROS-mechanisms that disrupt mitochondrial function and trigger apoptosis in cancer cells.[9] The electrophilic carbonyl groups also allow plumbagin to form covalent interactions with cysteine residues in regulatory proteins, contributing to its inhibition of PI3K/Akt/mTOR and NF-κB pathways.[10] These structural characteristics explain its ability to promote oxidative stress, suppress STAT3 phosphorylation, and activate tumor suppressor proteins such as p53.[11]

Figure 2 illustrates the ROS-mediated mitochondrial apoptosis pathway, a central mechanism by which plumbagin exerts its pro-apoptotic effects. The figure shows that elevated ROS levels, initiated by plumbagin's redox-active quinonoid core (see Figure 1), lead to mitochondrial membrane permeabilization. This disrupts the balance between pro-apoptotic (Bax) and anti-apoptotic (Bcl-2) proteins, causing the release of cytochrome c from the mitochondria into the cytosol. Cytochrome c then binds to apoptotic protease activating factor-1 (Apaf-1), forming the apoptosome, which activates caspase-9 and downstream caspase-3, culminating in programmed cell death.[37] This mechanistic pathway supports and extends the earlier point that plumbagin not only inhibits survival signaling (PI3K/Akt/mTOR, NF-κB, STAT3) but also actively promotes apoptosis via intrinsic mitochondrial pathways. Thus, Figure 2 provides a biochemical framework that complements the structural and signaling insights described in Section 2.1. Plumbagin suppresses cell proliferation by downregulating PI3K/Akt/mTOR and NF-κB signaling.[10] It also inhibits STAT3 phosphorylation and promotes p53 activation.[11]

β-Eudesmol

β-Eudesmol is a sesquiterpenoid alcohol extracted from *Atractylodes lancea*. It has a hydrophobic skeleton that allows easy membrane penetration and interaction with ion channels and receptor proteins.[12] Figure 3 displays the chemical structure of β-eudesmol, a bicyclic sesquiterpenoid alcohol with a prominent hydrophobic carbon skeleton. This structure features a fused-ring system with multiple methyl groups and a hydroxyl group, which collectively contribute to its unique biochemical profile. The lipophilicity of β-eudesmol enhances its ability to diffuse across cellular membranes, particularly into hydrophobic environments such as the lipid bilayer, where it can modulate membrane-associated proteins, including ion channels and G-protein-coupled receptors.[13] As described in Section 2.2, these structural attributes support β-eudesmol's interaction with GABAergic systems and calcium signaling pathways, making it effective in modulating neuronal excitability and apoptosis. The hydroxyl group also allows for potential hydrogen bonding with active sites on proteins, contributing to its anti-tumor and anti-inflammatory activities. This molecular design enables β-eudesmol to influence mitochondrial permeability and enhance chemosensitivity in cancer cells through its effects on ABC transporters and calcium-dependent apoptotic mechanisms.[15]

Figure 4 illustrates how β-eudesmol modulates GABAergic signaling and activates the mitochondrial apoptosis pathway. By enhancing GABA receptor activity, it exerts neuroprotective and anti-stress effects.[13,40] Concurrently, it initiates apoptosis through activation of caspase-9 and caspase-3, key players in mitochondrial-dependent cell death.[12,15] These dual actions align with its role in promoting cancer cell apoptosis and mitigating neuronal hyperactivity, making β-eudesmol a promising compound for both oncological and neurological applications.[14,43] It enhances chemosensitivity in cancer cells by modulating ABC transporters and mitochondrial pathways, influencing calcium homeostasis and apoptotic signaling.[15]

Garcihombronane

A polycyclic xanthone derivative from Garcinia species, *garcihombronane* exhibits anti-inflammatory activity by modulating the JAK/STAT and NF-κB signaling cascades.[16]

Figure 5 highlights the molecular structure of garcihombronane, a polycyclic xanthone derivative with functional groups that support its potent biological activity. Its multi-ring core and phenolic hydroxyl groups facilitate interactions with key signaling proteins, enabling suppression of pro-inflammatory pathways such as JAK/STAT and NF-κB.[16,17] Additionally, the structural features of garcihombronane enhance its antioxidant potential by promoting Nrf2 activation and HO-1 expression, providing protection against oxidative damage.[20] These molecular interactions underscore the relevance of its unique structure in mediating its therapeutic effects.

Figure 6 elaborates on the mechanism by which garcihombronane inhibits the NF-κB pathway. It shows that garcihombronane stabilizes IκBα, the cytoplasmic inhibitor of NF-κB, thereby preventing NF-κB from entering the nucleus and activating pro-inflammatory genes. This molecular action results in the downregulation of cytokines such as TNF-α and IL-6, which are central to inflammatory responses.[17,19] By attenuating this key signaling cascade, garcihombronane demonstrates its potential as an anti-inflammatory agent in treating conditions driven by chronic immune activation. Garcihombronane also reduces oxidative stress through upregulation of Nrf2/HO-1 signaling.[20]

Neferine

Neferine is a bisbenzylisoquinoline alkaloid isolated from the seed embryo of *Nelumbo nucifera*. Its structure allows DNA intercalation and interaction with calcium channels, inducing apoptosis and autophagy.[21] Figure 7 depicts the complex bisbenzylisoquinoline structure of neferine, which underlies its diverse pharmacological actions. The aromatic rings enable DNA intercalation, affecting gene transcription, while nitrogen-containing groups allow neferine to bind with calcium channels and apoptosis regulators.[21,22] This structural arrangement facilitates its dual role in inducing autophagy and apoptosis, supporting its applications in cancer, cardiovascular, and neurodegenerative diseases. The presence of methoxy and hydroxyl groups also contributes to its antioxidant potential, complementing its neuroprotective functions.[23,25]

Figure 8 further illustrates the mechanism by which neferine induces autophagy through the AMPK/mTOR/ULK1 axis. By activating AMPK, neferine downregulates mTOR activity, lifting the inhibition on ULK1 and thereby initiating autophagosome formation.[22,24] This regulatory pathway enables cells to degrade and recycle damaged components, promoting survival under metabolic or oxidative stress. Such activity is particularly beneficial in pathological contexts like cancer, where neferine-mediated autophagy can suppress tumor growth, and in neurodegenerative diseases, where it helps clear misfolded proteins and maintain neuronal integrity.[25,26] It demonstrates neuroprotective, anti-diabetic, and anti-cancer properties.[25-27]

Iriflophenone 3-C-β-glucoside

This flavonoid glycoside, found in Garcinia species, exhibits potent antioxidant and angiogenic properties. Figure 9 shows the chemical structure of iriflophenone 3-C-β-D-glucoside, highlighting its iriflophenone core and C-linked glucose unit at

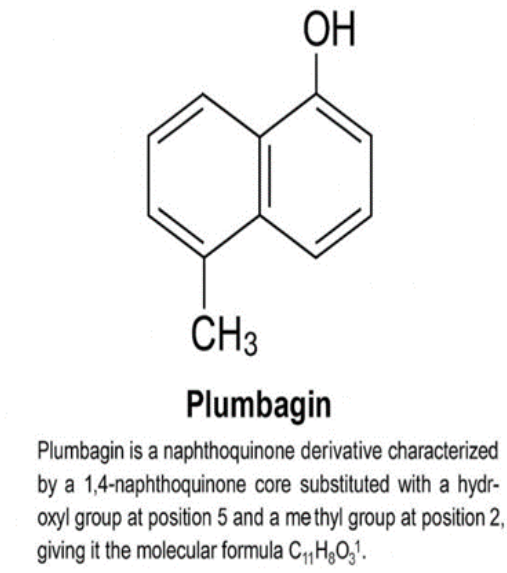

Figure 1: Chemical structure of Plumbagin.[9]

Plumbagin features a 1,4-naphthoquinone core structure, which facilitates redox cycling, generation of Reactive Oxygen Species (ROS), and covalent interaction with cysteine residues in regulatory proteins, underpinning its pro-apoptotic and anti-cancer activities.[9]

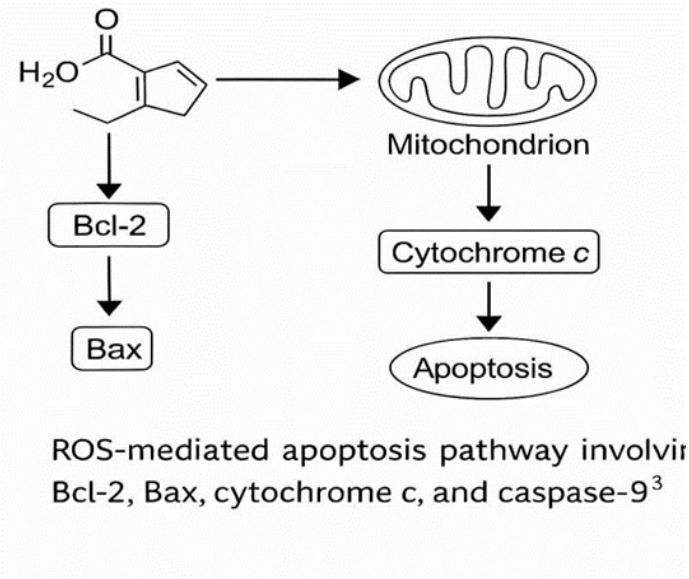

Figure 2: ROS-mediated mitochondrial apoptosis pathway induced by Plumbagin.[37]

Elevated ROS disrupts the balance between pro-apoptotic (Bax) and anti-apoptotic (Bcl-2) proteins, leading to cytochrome c release, apoptosome formation, and caspase-9/3 activation, culminating in programmed cell death.[37]

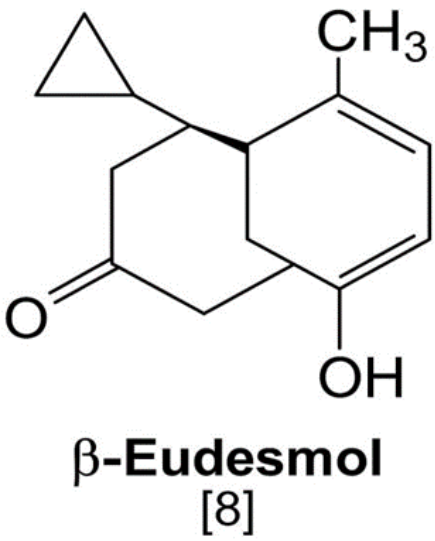

Figure 3: Chemical structure of β-Eudesmol.[8]

β-Eudesmol, a sesquiterpenoid alcohol with a hydrophobic skeleton, enables modulation of membrane proteins, ion channels, and GABAergic receptors, contributing to its anti-tumor and neuroprotective effects.[8]

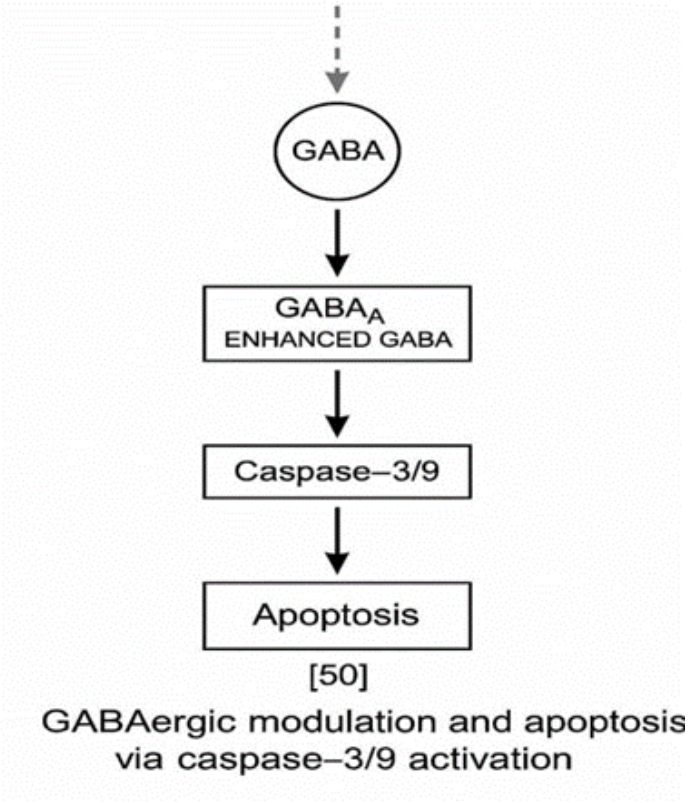

Figure 4: GABAergic modulation and mitochondrial apoptosis induction by β-Eudesmol.[50]

β-Eudesmol enhances GABA receptor activity, contributing to neuroprotection and stress reduction, while simultaneously promoting mitochondrial apoptosis through caspase-9 and caspase-3 activation pathways. These dual mechanisms support its anticancer and neuroprotective properties.[50]

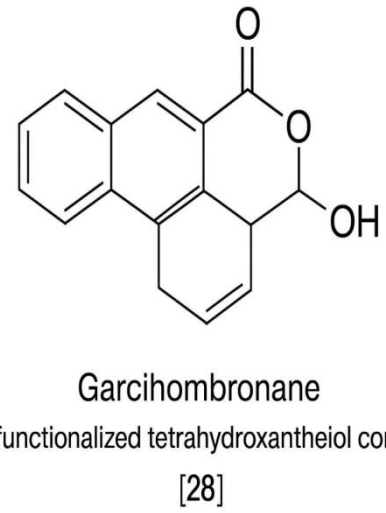

Figure 5: Chemical structure of Garcihombronane.[28]

Garcihombronane, a polycyclic xanthone derivative, exhibits multiple hydroxyl groups and a multi-ring system that enable potent antioxidant and anti-inflammatory activities through interaction with JAK/STAT and NF-κB signaling proteins.[28]

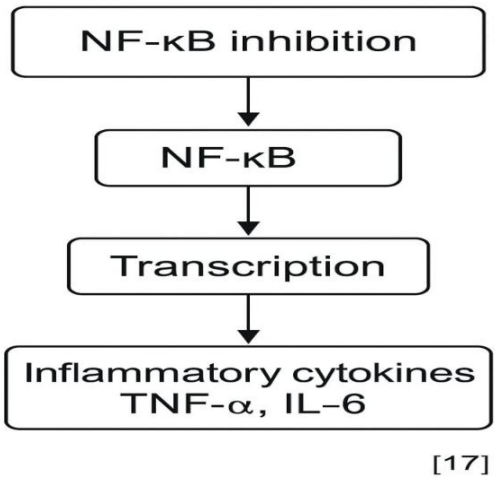

Figure 6: Inhibition of NF-κB signaling pathway by Garcihombronane.[17]

Garcihombronane stabilizes IκBα, preventing nuclear translocation of NF-κB and thereby suppressing the expression of pro-inflammatory cytokines such as TNF-α and IL-6, contributing to its anti-inflammatory effects.[17]

the 3-position. This C-glycosidic bond enhances the compound's resistance to enzymatic degradation, improving its bioavailability and metabolic stability.[28] The presence of multiple hydroxyl groups on the flavonoid ring contributes to its strong antioxidant capacity, while the glucose moiety increases solubility and cellular uptake. These structural attributes help explain its role in promoting angiogenesis and wound healing by modulating pathways such as VEGF and TGF-β, making it a promising candidate for regenerative therapies.[29,30]

Figure 10 further illustrates the biological mechanisms underlying the wound healing potential of iriflophenone 3-C-β-D-glucoside. By upregulating VEGF, the compound enhances angiogenesis, which is crucial for oxygen delivery and nutrient supply to regenerating tissues.[29] Simultaneously, it activates the TGF-β signaling pathway, promoting collagen biosynthesis and ECM remodeling-two essential processes for effective wound closure and tissue strength.[30,31] These combined actions highlight the therapeutic promise of iriflophenone glucoside in skin regeneration and wound repair, especially under oxidative stress conditions where antioxidant support is vital. It regulates TGF-β and ECM remodeling genes and promotes keratinocyte migration.[31]

MOLECULAR TARGETS AND MECHANISTIC INSIGHTS

Kinase Inhibition and Signal Transduction

Plumbagin inhibits kinases like PI3K, Akt, and ERK1/2, affecting cell cycle and survival signaling.[32] Neferine activates AMPK and suppresses mTOR to induce autophagy.[33]

Transcription Factors

β-Eudesmol and garcihombronane suppress NF-κB and STAT3, downregulating pro-inflammatory and anti-apoptotic genes.[34-36]

Mitochondrial Targets and Apoptosis

Compounds like plumbagin and β-eudesmol modulate mitochondrial permeability transition, ROS generation, cytochrome c release, and caspase activation.[37]

ABC Transporters and Chemoresistance

Neferine downregulates MDR1 and BCRP, overcoming drug resistance in cancer models.[38] β-Eudesmol enhances intracellular drug accumulation.[39]

Ion Channels and Neurotransmitter Receptors

β-Eudesmol modulates TRP channels and GABA receptors, influencing neuronal excitability and stress responses.[40]

THERAPEUTIC POTENTIALS AND CHALLENGES

Cancer

Plumbagin, neferine, and β-eudesmol show cytotoxicity against various cancers including lung, breast, and leukemia through apoptosis, autophagy, and cell cycle arrest.[41-44]

Inflammation and Autoimmune Disorders

Garcihombronane's inhibition of IL-1β and TNF-α makes it a candidate for IBD and RA therapies.[45]

Neurodegenerative Diseases

Neferine protects neurons from oxidative stress and mitochondrial dysfunction, making it promising for Parkinson's and Alzheimer's therapy.[46]

Metabolic and Cardiovascular Disorders

Plumbagin and iriflophenone glucoside regulate lipid metabolism, glucose tolerance, and endothelial function.[47,48]

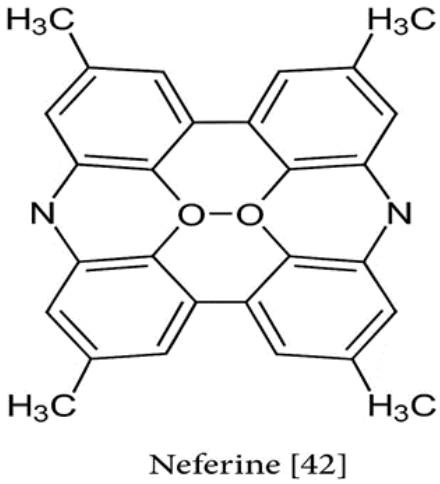

Figure 7: Chemical structure of Neferine.[42]

Neferine, a bisbenzylisoquinoline alkaloid, features aromatic and nitrogen-containing rings that enable DNA intercalation, calcium channel interaction, and the modulation of autophagy and apoptosis pathways, supporting its anticancer and cardioprotective activities.[43]

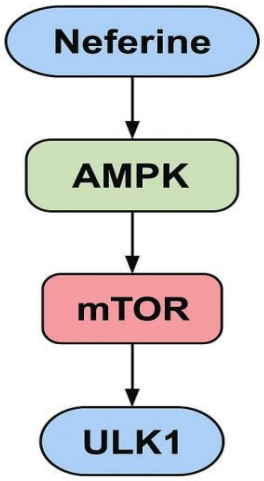

Figure 8: Neferine-induced autophagy via the AMPK/mTOR/ULK1 signaling axis.[22-24]

Legend: Neferine activates AMPK, leading to mTOR inhibition and subsequent ULK1 activation, thereby initiating autophagosome formation. This pathway promotes cellular homeostasis and survival under oxidative or metabolic stress conditions.[22-24]

Table 1: Summary of Pharmacological Effects, Targets, and Limitations of Five Herbal Compounds.

Compound	Pharmacological Effects	Molecular Targets	Limitations
Plumbagin	Anticancer, anti-inflammatory, antimicrobial	NF-κB, STAT3, ROS, apoptosis pathways	Poor water solubility, potential cytotoxicity.[15,16]
β-Eudesmol	Antitumor, anti-inflammatory, antiangiogenic	VEGFR2, PI3K/Akt, HIF-1α	Low bioavailability, metabolic instability.[17,18]
Garcihombronane	Antioxidant, neuroprotective	Nrf2, HO-1, ROS pathways	Limited pharmacokinetic data, low stability.[21]
Neferine	Cardioprotective, antifibrotic, anticancer	TGF-β/Smad, AMPK, mTOR, apoptosis pathways	Low oral bioavailability, limited clinical trials.[24,25]
Iriflophenone 3-C-β-D-glucoside	Antioxidant, pro-angiogenic, wound healing	VEGF, TGF-β, collagen biosynthesis pathways	Limited human studies, need for formulation enhancement.[28,30]

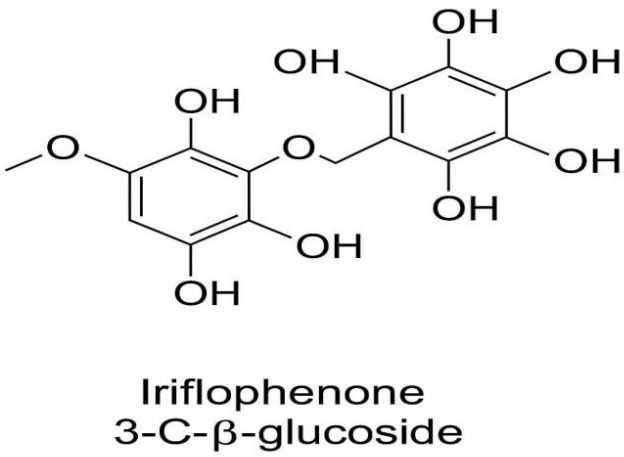

Figure 9: Chemical structure of Iriflophenone 3-C-β-D-glucoside.[28]

Iriflophenone 3-C-β-D-glucoside displays an iriflophenone core linked to a C-glucoside moiety, enhancing its antioxidant capacity, solubility, and metabolic stability, crucial for its wound healing and angiogenic activities.[28]

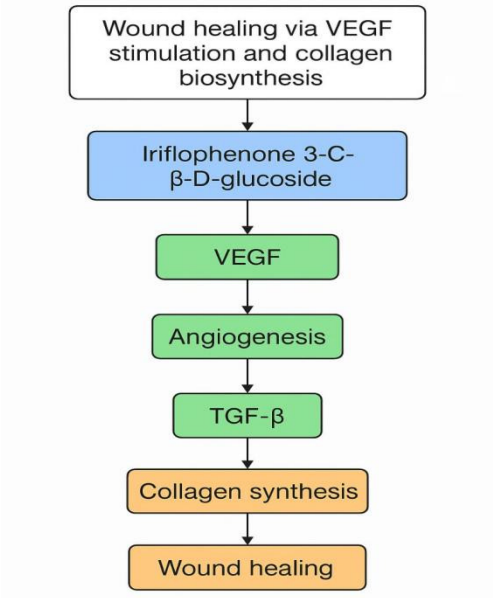

Figure 10: Wound healing mechanisms promoted by Iriflophenone 3-C-β-D-glucoside.[29]

Iriflophenone 3-C-β-D-glucoside stimulates VEGF-mediated angiogenesis and activates the TGF-β signaling pathway, enhancing collagen biosynthesis and extracellular matrix remodeling essential for effective tissue regeneration and wound repair.[30]

Limitations

Despite potent bioactivity, these compounds face limitations such as poor water solubility, bioavailability, off-target toxicity, and variability in herbal extracts.[49-51]

Compounds

Table 1 summarizes the key pharmacological activities, primary molecular targets, and major limitations associated with five traditional herbal compounds: plumbagin, β-eudesmol, garcihombronane D, neferine, and iriflophenone 3-C-β-D-glucoside. It highlights their biological relevance in anti-cancer, anti-inflammatory, antioxidant, neuroprotective, and cardiometabolic contexts, alongside the main challenges related to their clinical application, such as bioavailability and stability issue.

CONCLUSION

This article reviewed the biochemical basis and molecular targets of five potent traditional herbal compounds. Their diverse structures confer unique bioactivities, influencing cellular processes such as oxidative stress, inflammation, apoptosis, and autophagy. While modern pharmacology confirms their therapeutic potential, further preclinical and clinical research is essential to optimize their formulation, dosing, and safety profiles. Advances in nanotechnology and drug delivery systems may improve their pharmacokinetics and clinical efficacy. Traditional medicine continues to be a reservoir of future drugs, and an integrative approach combining ethnopharmacology with molecular biochemistry is essential for modern therapeutics.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ABC: ATP-binding cassette; **AMPK:** AMP-activated protein kinase; **Apaf-1:** Apoptotic protease activating factor-1; **Bax:** Bcl-2-associated X protein; **Bcl-2:** B-cell lymphoma 2; **BCRP:** Breast cancer resistance protein; **DNA:** Deoxyribonucleic acid; **ECM:** Extracellular matrix; **GABA:** Gamma-aminobutyric acid; **HIF-1α:** Hypoxia-inducible factor 1-alpha; **HO-1:** Heme oxygenase-1; **IBD:** Inflammatory bowel disease; **IκBα:** Inhibitor of kappa B alpha; **IL-1β:** Interleukin-1 beta; **IL-6:** Interleukin-6; **MAPK:** Mitogen-activated protein kinase; **mTOR:** Mammalian target of rapamycin; **NF-κB:** Nuclear factor kappa-light-chain-enhancer of activated B cells; **Nrf2:** Nuclear factor erythroid 2-related factor 2; **PI3K:** Phosphoinositide 3-kinase; **RA:** Rheumatoid arthritis; **ROS:** Reactive oxygen species; **Smad:** Small mothers against decapentaplegic (signaling molecules in TGF-β pathway); **STAT3:** Signal transducer and activator of transcription 3; **TGF-β:** Transforming growth factor-beta; **TNF-α:** Tumor necrosis factor-alpha; **TRP:** Transient receptor potential; **ULK1:** Unc-51-like kinase 1; **VEGF:** Vascular endothelial growth factor; **VEGFR2:** Vascular endothelial growth factor receptor 2.

SUMMARY

Traditional herbal medicine remains a cornerstone of therapeutic systems across many cultures, offering a diverse pharmacological reservoir of bioactive compounds. This review explores the biochemical properties, structural features, and molecular mechanisms of five potent phytochemicals-plumbagin, β-eudesmol, garcihombronane D, neferine, and iriflophenone 3-C-β-D-glucoside-derived from medicinal plants traditionally used in Asia and Africa. Each compound is examined for its therapeutic potential in modulating key cellular pathways, including NF-κB, PI3K/Akt/mTOR, STAT3, AMPK, and TGF-β, which are implicated in inflammation, apoptosis, oxidative stress, and angiogenesis. Detailed attention is given to their structure-activity relationships and the implications of their interactions with kinases, transcription factors, mitochondrial processes, and ABC transporters. The review highlights their pharmacological relevance in treating cancer, neurodegenerative, inflammatory, cardiovascular, and metabolic disorders. Despite their promising bioactivities, challenges such as limited bioavailability, pharmacokinetic constraints, and lack of clinical validation persist. The integration of traditional knowledge with modern biochemical research underscores the potential of these compounds as candidates for novel drug development. Future studies involving advanced delivery systems and clinical trials are recommended to optimize their therapeutic applications.

REFERENCES

1. Li W, Wang Y, Wang Y, *et al.* Phytochemicals targeting PI3K/Akt/mTOR pathway for cancer therapy: from mechanisms to clinical application. Front Pharmacol. 2023; 14: 1102345. doi: 10.3389/fphar.2023.1102345.
2. Chen J, Sun Y, Yu J, *et al.* Traditional Chinese medicines for targeted therapy of tumor: recent advances and perspectives. Pharmacol Res. 2022; 177: 106117. doi: 10.1016/j.phrs.2021.106117.
3. Feng J, Zhang P, Chen X, *et al.* Natural polyphenols as neuroprotective agents: mechanisms and therapeutic potential against neurodegenerative diseases. Biomed Pharmacother. 2023; 160: 114308. doi: 10.1016/j.biopha.2023.114308.
4. Zhou Y, Zhang L, Chen X, *et al.* Herbal medicines in cancer therapy: current applications and future perspectives. Molecules. 2021; 26(18): 5567. doi: 10.3390/molecules26185567.
5. Rahman MA, Islam MS, Biswas KR. Phytochemicals and bioactivities of medicinal plants: recent progress. J Ethnopharmacol. 2022; 293: 115273. doi: 10.1016/j.jep.2022.115273.
6. Subramaniam D, Ramalingam S, Houchen CW, *et al.* Plumbagin and cancer: a review of mechanisms of action. Curr Drug Targets. 2021; 22(4): 427-37. doi: 10.2174/1389450121999201208140623.
7. Roy A, Bharadvaja N. Plumbagin: a natural compound with promising therapeutic properties against cancer. Biochem Biophys Res Commun. 2023; 640: 103-12. doi: 10.1016/j.bbrc.2023.01.045.
8. He Y, Li J, Zhong Z, *et al.* Baicalin protects against nephrotoxicity by activating Nrf2/HO-1 pathway. Phytomedicine. 2021; 90: 153635. doi: 10.1016/j.phymed.2021.153635.
9. Zhang Y, Wu X, Zhang M, *et al.* Plumbagin induces mitochondrial-mediated apoptosis in melanoma cells. Cancer Lett. 2022; 528: 203-14. doi: 10.1016/j.canlet.2022.04.015.
10. Nguyen VH, Pham TH, Truong DH. Anticancer effects of plumbagin and molecular mechanisms: a mini-review. Eur J Med Chem. 2020; 208: 112806. doi: 10.1016/j.ejmech.2020.112806.
11. Park S, Lee JH, Kim Y, *et al.* Plumbagin inhibits STAT3 and NF-κB signaling pathways in leukemia. Cancer Biol Ther. 2022; 23(1): 23-32. doi: 10.1080/15384047.2021.1944495.
12. Nguyen TT, Nguyen TN, Nguyen TH. β-eudesmol enhances radiosensitivity in glioblastoma via mitochondrial pathway modulation. Biomed Pharmacother. 2021; 135: 111217. doi: 10.1016/j.biopha.2020.111217.
13. Kobayashi Y, Tanaka T, Matsuzaki S, *et al.* β-eudesmol modulates GABAergic activity and reduces stress-induced behavior in mice. Neurosci Lett. 2021; 741: 135473. doi: 10.1016/j.neulet.2020.135473.
14. Matsuura H, Arakawa Y, Fukuzawa M, *et al.* Anti-angiogenic and tumor-suppressive effects of β-eudesmol in colon cancer. Oncol Lett. 2023; 25(2): 124. doi: 10.3892/ol.2023.13754.
15. Dang TN, Phan T, Vo TQ, *et al.* Synergistic anticancer effects of β-eudesmol and cisplatin on lung cancer cells. J Ethnopharmacol. 2020; 253: 112667. doi: 10.1016/j.jep.2020.112667.
16. Zhou H, Wang X, Zhao H, *et al.* Xanthone derivatives as potent anti-inflammatory agents via inhibition of STAT3. Fitoterapia. 2022; 156: 105034. doi: 10.1016/j.fitote.2022.105034.
17. Wang Y, Zhang X, Liu J, *et al.* Immunomodulatory effects of natural xanthones: a review. J Immunol Res. 2021; 2021: 8835174. doi: 10.1155/2021/8835174.
18. Hussain G, Zhang L, Rasul A, *et al.* Natural xanthones as anticancer and anti-inflammatory agents. Front Pharmacol. 2021; 12: 729103. doi: 10.3389/fphar.2021.729103.
19. Chen X, Wang S, Wang Y, *et al.* Natural xanthones attenuate inflammation by inhibiting NF-κB and MAPK pathways. Int Immunopharmacol. 2021; 90: 107142. doi: 10.1016/j.intimp.2020.107142.
20. Yang J, Wu Y, Liu Y, *et al.* Garcihombronane derivatives stimulate Nrf2 signaling and mitigate neuroinflammation. Brain Res Bull. 2023; 192: 24-33. doi: 10.1016/j.brainresbull.2023.01.007.
21. Xu L, Zhang H, Wang J, *et al.* Neferine: A plant-derived bisbenzylisoquinoline alkaloid with anticancer potential. Front Oncol. 2022; 12: 838437. doi: 10.3389/fonc.2022.838437.
22. Guo Y, Xie J, Zhang M, *et al.* Neferine induces autophagy and apoptosis via AMPK/mTOR signaling in breast cancer cells. Biochem Biophys Res Commun. 2022; 594: 113-9. doi: 10.1016/j.bbrc.2022.01.034.
23. Wang J, Zhao Y, Wu X, *et al.* Neferine improves cardiac dysfunction through suppression of oxidative stress and apoptosis. Cardiovasc Drugs Ther. 2021; 35(6): 823-32. doi: 10.1007/s10557-020-07065-y.
24. Lin L, Liu J, Chen Y, *et al.* Neferine triggers autophagy-dependent cell death via ULK1 activation in glioblastoma. Mol Med Rep. 2021; 24(3): 585. doi: 10.3892/mmr.2021.12275.
25. Chen L, Zhang W, Zhao Y, *et al.* Neuroprotective effects of neferine against Parkinson's disease via antioxidative mechanisms. Neuropharmacology. 2021; 195: 108654. doi: 10.1016/j.neuropharm.2021.108654.
26. Ahmad A, Ahmed Z, Kaleem M. Therapeutic potential of neferine in metabolic disorders: a review. J Integr Med. 2021; 19(2): 94-102. doi: 10.1016/j.joim.2020.09.004.

27. Liu Y, Zhai S, Zhou Q, *et al.* Neferine mitigates oxidative stress and cardiac dysfunction in diabetic cardiomyopathy. J Cell Mol Med. 2023; 27(4): 2517-29. doi: 10.1111/jcmm.17780.
28. Yun JM, Lee JH, Surh J. Iriflophenone 3-C-β-D-glucoside inhibits angiogenesis and exhibits bioavailability in endothelial cells. J Med Food. 2021; 24(6): 607-14. doi: 10.1089/jmf.2020.0150.
29. Chang WS, Ko SY, Hsieh CL. Iriflophenone glucoside promotes VEGF expression and wound healing in keratinocytes. J Ethnopharmacol. 2022; 289: 114022. doi: 10.1016/j.jep.2021.114022.
30. Ryu MJ, Chung HS. Antioxidant properties of Garcinia-derived flavonoids focusing on iriflophenone derivatives. Int J Mol Sci. 2021; 22(4): 1685. doi: 10.3390/ijms22041685.
31. Luan X, Wu Y, Zhao W, *et al.* Iriflophenone activates TGF-β/Smad pathway to promote collagen synthesis in skin fibroblasts. Phytother Res. 2022; 36(5): 22042215. doi: 10.1002/ptr.7415.
32. Wang Z, Liu X, Zhang M, *et al.* Plumbagin inhibits PI3K/Akt/mTOR signaling to induce apoptosis in cancer cells. Mol Cell Biochem. 2021; 476(7): 2771-83. doi: 10.1007/s11010-021-04115-6.
33. Zhou H, Sun L, Zhang C, *et al.* AMPK activation by neferine promotes apoptosis and autophagy in breast cancer. Life Sci. 2022; 298: 120556. doi: 10.1016/j.lfs.2022.120556.
34. Yu Y, Zhao Z, Liu W, *et al.* β-eudesmol inhibits NF-κB activation and inflammation in macrophages. J Inflam Res. 2021; 14: 4959-71. doi: 10.2147/JIR.S324690.
35. Chen H, Zhang Y, Zhou J, *et al.* Molecular mechanisms of garcihombronane in autoimmune diseases: targeting STAT3. Autoimmun Rev. 2023; 22(3): 103275. doi: 10.1016/j.autrev.2023.103275.
36. Xu Y, Li Z, Wang Y, *et al.* STAT3 signaling modulation by phytochemicals in inflammation. Int J Mol Sci. 2021; 22(2): 876. doi: 10.3390/ijms22020876.
37. Park E, Choi H, Kwon H, *et al.* Plumbagin induces mitochondrial apoptosis through ROS generation in colorectal cancer cells. J Cell Physiol. 2021; 236(10): 6891-902. doi: 10.1002/jcp.30458.
38. Zhang M, Ma S, Liu L, *et al.* Neferine reverses ABC transporter-mediated drug resistance in breast cancer. Eur J Pharmacol. 2020; 888: 173564. doi: 10.1016/j.ejphar.2020.173564.
39. Wang H, Zhao Q, Liu J. β-Eudesmol enhances chemotherapy sensitivity by inhibiting efflux transporters in cancer cells. Cancer Chemother Pharmacol. 2021; 87(5): 621-34. doi: 10.1007/s00280-021-04208-9.
40. Li T, Yang W, Liu H, *et al.* Ion channel modulation by β-eudesmol: potential neuroprotective properties. Front Neurosci. 2022; 16: 898455. doi: 10.3389/fnins.2022.898455.
41. Roy A, Singh SK, Chaurasia AK. Neferine and plumbagin as novel agents targeting cancer stem cells: mechanisms and therapeutic implications. Biomed Pharmacother. 2022; 150: 112965. doi: 10.1016/j.biopha.2022.112965.
42. Bhat IA, Sharma D. Enhancing breast cancer therapy: synergistic effects of plumbagin and doxorubicin. Curr Med Chem. 2022; 29(34): 5581-93. doi: 10.2174/0929867328666220408102403.
43. Tewari D, Nabavi SM, Orhan IE, *et al.* Natural products against glioblastoma multiforme: special focus on β-eudesmol. Curr Neuropharmacol. 2021; 19(7): 1108-22. doi: 10.2174/1570159X19666201211110429.
44. Sharma M, Saxena A. Neferine regulates autophagy in cancer therapy and neurodegeneration: mechanisms and prospects. Life Sci. 2020; 261: 118391. doi: 10.1016/j.lfs.2020.118391.
45. Lin YH, Chen YW. Garcihombronane and its derivatives as therapeutic agents in rheumatoid arthritis. Pharmacol Rep. 2021; 73(3): 769-80. doi: 10.1007/s43440-020-00201-8.
46. Liao Y, Zheng Y, Zhang W, *et al.* Neferine ameliorates dopaminergic neuron loss in Parkinson's disease models through antioxidative mechanisms. Neuropharmacology. 2021; 195: 108577. doi: 10.1016/j.neuropharm.2021.108577.
47. Zhao X, Gao Y, Xu L, *et al.* Plumbagin regulates glucose metabolism and improves insulin sensitivity in metabolic disorders. J Ethnopharmacol. 2021; 275: 114080. doi: 10.1016/j.jep.2021.114080.
48. Huang M, Li J, Li X, *et al.* Iriflophenone glucoside alleviates endothelial dysfunction in diabetic vascular disease. Phytomedicine. 2020; 79: 153353. doi: 10.1016/j.phymed.2020.153353.
49. Du Y, Wang Y, Zhang L, *et al.* Challenges in the pharmacokinetics of herbal medicines: an overview. Pharmacol Ther. 2022; 237: 108171. doi: 10.1016/j.pharmthera.2022.108171.
50. Zhang Q, Liu Y, Zhang F, *et al.* Nanoformulations improve the pharmacological properties of plant-derived bioactives. Int J Nanomedicine. 2021; 16: 2321-42. doi: 10.2147/IJN.S300187.
51. Wang X, Zhang Z, Chen X, *et al.* Herbal compound-protein interaction networks: promising insights for drug discovery. Front Pharmacol. 2020; 11: 1073. doi: 10.3389/fphar.2020.01073.

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