



SYNERGISTIC POTENTIAL OF CURCUMIN AND BERBERINE: FROM PLANT-ORIGIN COMPOUNDS TO NANOPARTICLE-ENABLED THERAPEUTICS

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ABSTRACT

Curcumin, a polyphenolic diarylheptanoid derived from *Curcuma longa* (turmeric), and berberine, an isoquinoline alkaloid prevalent in *Berberis aristata* (Indian barberry), are two powerful bioactive chemicals of plant origin, exhibiting significant antibacterial, anti-inflammatory, and anticancer activities. This review examines the botanical origins, chemical characteristics, principle pharmacological qualities, and significant limitations—specifically inadequate aqueous solubility and limited oral bioavailability that hinder clinical applications. Recent research underscores the synergistic effects of curcumin and berberine, especially in cancer therapy, where their co-administration yields enhanced growth inhibition and apoptosis in cancer cell models, surpassing the efficacy of single-compound treatment. Moreover, breakthroughs in nanotechnology have facilitated the creation of nanoparticles and nanocomposites loaded with curcumin and berberine, including silver-curcumin and silver-berberine composites, which markedly enhance bioavailability and therapeutic efficacy. This study elucidates the prospective applications of these phytochemicals in contemporary medicine, highlighting their significance in the advancement of novel nanoparticle-based therapeutics.

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INTRODUCTION

Plants have long been a source of bioactive compounds with potent antimicrobial and anticancer properties (Prasad et al., 2014). Traditional medicinal plants like *Curcuma longa* (turmeric) and *Berberis aristata* (Indian barberry) contain powerful phytochemicals such as curcumin and berberine, respectively. These compounds exhibit a wide range of therapeutic effects, including antibacterial, antiviral, anti-inflammatory, and anticancer activities (Prasad et al. 2014; Gupta et al. 2013; Sharma et al. 2011). Recent pharmacological studies indicate that combination therapy using plant-derived compounds can enhance therapeutic efficacy via synergistic mechanisms, particularly in cancer treatment (Maria Younes

et al., 2022; Giordano & Tommonaro, 2019; Catanzaro et al., 2018).

Botanical Sources and Ethnomedicinal Significance

Curcuma longa & Curcumin: Turmeric, scientifically known as *Curcuma longa*, belongs to the Zingiberaceae family. The brilliant yellow rhizomes are extensively utilized as a spice and in traditional medicine in India, China, and Indonesia (Gupta et al. 2013; Wang et al. 2021). Curcumin is the primary compound in turmeric responsible for its distinctive hue and health advantages. Turmeric has been utilized in Ayurvedic medicine for centuries due to its anti-inflammatory properties, cellular protection, and anticancer effects (Modaresi et al. 2017; Wang et al., 2021).

Berberis aristata & berberine: *Berberis aristata*, known as “Daru Haldi,” is a spiny shrub native to the Northern Himalayan region (Sharma et al. 2011). Berberine, an isoquinoline alkaloid present in the roots and bark, constitutes the primary bioactive molecule in *B. aristata*. Berberine has historically

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been utilized for its antibacterial properties, anti-inflammatory effects, and anticancer potential (Suliman et al. 2022). This plant remains a significant source of pharmacologically active chemicals utilized in contemporary medicine.

Chemical Nature and Structural Characteristics:

Curcumin: Curcumin, chemically known as diferuloylmethane, has the IUPAC name (1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione and a molecular formula of $C_{21}H_{20}O_6$ (Kamran et al., 2020; Nurjanah & Saepudin, 2019). Curcumin contains two aromatic rings connected by a seven-carbon linker, with methoxy and hydroxyl groups contributing to its antioxidant & anticancer activities (Priyadarsini, 2014). Bright yellow color of the curcumin is because of the presence of polyphenol. Phenolic hydroxyl and methoxy groups enable interaction with multiple cellular targets (Nelson et al., 2017). Turmeric also contains volatile oils such as ar-turmerone and zingiberone that may synergize with curcumin's bioactivity (Gupta et al., 2013).

Berberine: Berberine is an isoquinoline alkaloid with the molecular formula $C_{20}H_{18}NO_4$ (Yao et al., 2018). Berberine's structure includes a planar quaternary ammonium group, which is crucial for its antimicrobial and anticancer activities (Suliman Khan et al., 2022). This structural uniqueness allows berberine to interact with various biological targets effectively.

Historical Significance and Therapeutic Potential:

Curcumin: Curcumin, having nearly a two-centuries-old scientific history, continues to attract researchers worldwide. Isolated from turmeric (*Curcuma longa*) in 1815, its chemical structure, synthesis, and antioxidant activities were scarcely studied until the 1970s (Kavirayani Indira Priyadarsini, 2014). Over the long history of turmeric, curcumin—the primary pharmacological agent—has gained increasing recognition for its medicinal properties (Modaresi M et al., 2017). The demand for curcumin is rising due to its anti-inflammatory, antioxidant, and anticancer properties (Elisabetta Zerazion et al., 2016). Its desirable therapeutic effects are linked to its antioxidant and anti-inflammatory properties, combined with an outstanding pharmacological safety profile (Pulido-Moran M et al., 2016; Zorka Stanić, 2017).

Curcumin-nanoconjugates with cobalt and silver nanoparticles exhibit antimicrobial activity, with silver nanocomposites being developed for treating microbial infections (Kavirayani Indira Priyadarsini, 2014). Curcumin also functions as an antibiotic, antioxidant (Majed Alwadei et al., 2019; Kamran Mansouri et al., 2020), and anti-inflammatory agent (Satoskar et al., 1986; Majed Alwadei et al., 2019; Kamran Mansouri et al., 2020), showing potential in treating cancer, aging, diabetes, neurological, and cardiovascular diseases (Shanmugam MK et al., 2015; Mahmood Khudhayer Oglah et al., 2020; Deutch C. E., 2022).

Curcumin shows that it can fight cancer, bacteria, viruses, and inflammation (Shanmugam et al., 2015; Perrone et al., 2015). It modulates critical signaling pathways, including NF- κ B, MAPK, and PI3K/Akt, thereby regulating apoptosis, angiogenesis, and metastasis (Gallardo & Calaf, 2016; Kamran Mansouri et al., 2020). Curcumin has demonstrated therapeutic efficacy against cancer, diabetes, cardiovascular, and neurodegenerative diseases (Pulido-Moran et al., 2016;

Mahmood Oglah et al., 2020).

Berberine: Berberine—a bioactive alkaloid derived from *Berberis aristata*—demonstrates exceptional therapeutic potential due to its low toxicity, unique structure, and broad medicinal properties (Patel Pineshkumar S et al., 2019; Suliman Khan et al., 2022). Berberine is known for its antioxidant, anticancer (Pierpaoli E et al., 2013), anti-inflammatory (Shailja Choudhary et al., 2021), antibacterial, and antiviral effects (Suliman Khan et al., 2022). It effectively combats multidrug-resistant *Escherichia coli* (Bandyopadhyay S et al., 2013; Cheng Hu et al., 2020) and is traditionally used to treat inflammation, wound healing, skin diseases, menorrhagia, diarrhea, jaundice, and eye infections (Sharma Komal et al., 2011). Berberine also exhibits antibacterial activity against pathogens like *Helicobacter pylori*, *Staphylococcus aureus*, and methicillin-resistant strains (Hue Thi Nguyen et al., 2022). Additionally, berberine inhibits proliferation and metastasis in various cancers, including leukemia, colorectal, prostate, lung, glioma, and ovarian cancers (Muhammad Javed Iqbal et al., 2021).

Curcumin and berberine possess a broad spectrum of medicinal properties. Both compounds have demonstrated potential in treating chronic diseases such as diabetes, cardiovascular disorders, and cancer (Muhammad Javed Iqbal et al., 2021).

Limitations and Bioavailability Challenges

Despite potent biological activity, curcumin suffers from low aqueous solubility, rapid metabolism, and poor systemic bioavailability (Siviero et al., 2015). Berberine also exhibits limited oral absorption due to P-glycoprotein-mediated efflux and first-pass metabolism (Mehanny et al., 2016; Iqbal et al., 2021). These limitations necessitate advanced drug-delivery strategies.

Synergistic therapeutic potential of curcumin and berberine:

The combination of curcumin and berberine has shown synergistic anticancer effects through enhanced apoptosis, cell-cycle arrest, and autophagic cell death (Kai Wang et al., 2016). Studies indicate that these compounds, when used together, are more effective against cancer cell lines such as MCF-7 and MDA-MB-231 compared to when used alone (Akanksha Kashyap et al., 2022). Synergy is attributed to complementary modulation of oxidative stress, mitochondrial pathways, and oncogenic signaling cascades (Yao & Zhang, 2018; Maria Younes et al., 2022; Deutch C. E., et al., 2022)

Nanotechnology-Based Delivery Strategies:

Nanoparticles & Nanocomposites: Nanotechnology has revolutionized drug delivery by enhancing the bioavailability and efficacy of therapeutic compounds (Florian J. Heiligttag and Markus Niederberger, 2013). "Nanoparticles such as silver nanoparticles (AgNPs) are widely used for their antimicrobial, antifungal, and anti-inflammatory properties" (Murphy et al., 2015). Nanocomposites, which incorporate nanoparticles into a matrix, offer improved mechanical and biological properties.

Silver nanoparticles & their medicinal applications: Silver nanoparticles (AgNPs) are known for their broad-spectrum antimicrobial activity. AgNPs have shown efficacy in wound healing, scar less healing, and as antibacterial agents in clinical

settings (Karnani, R. L., & Chowdhary, 2013; Murphy et al., 2015).

Silver-curcumin composite: Curcumin-loaded silver nanoparticles (Cur-AgNPs) have demonstrated enhanced anticancer activity, particularly against breast cancer cell lines (S. Garg and A. Garg, 2018). The nanoscale formulation improves curcumin's stability and bioavailability, making it more effective as a therapeutic agent.

Silver-Berberine Composite: Berberine-loaded silver nanoparticles exhibit significant antibacterial activity, making them potential candidates for treating multidrug-resistant infections (Hue Thi Nguyen et al., 2022). This combination enhances berberine's absorption and efficacy, overcoming its low bioavailability when administered orally (Muhammad Javed Iqbal et al., 2021).

CONCLUSION AND FUTURE PERSPECTIVE

Curcumin and berberine, derived from *Curcuma longa* and *Berberis aristata* respectively, exhibit a remarkable spectrum of medicinal properties, including antioxidant, anti-inflammatory, antibacterial, antiviral, and anticancer effects. Their potential in treating chronic diseases such as diabetes, cardiovascular disorders, and cancer highlights their importance in both traditional and modern medicine (Prasad et al., 2014; Iqbal et al., 2021). The development of nanoparticle-based formulations, such as silver-curcumin and silver-berberine composites, further enhances their therapeutic efficacy by improving bioavailability and stability. Continued research into these natural compounds and their synergistic applications holds promise for innovative and effective treatments in the pharmaceutical industry.

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