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The Therapeutic Potential of Turmeric/Curcumin for Uterine Fibroids

Francis Appiah*
Doctor of Naturopathic Medicine (N.D. Candidate), Medical Journalist, & Medical Laboratory Technologist

***Corresponding author:** Francis Appiah, Doctor of Naturopathic Medicine (N.D. Candidate), Medical Journalist, & Medical Laboratory Technologist

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Abstract

Imagine enduring years of excruciating menstrual cramps, heavy bleeding, and fertility struggles – a harsh reality for millions of women suffering from uterine fibroids. These benign tumors, common among women of reproductive age, cause significant morbidity and impact quality of life due to hormonal, growth factor, and inflammatory influences. Despite available treatments like surgery and hormonal therapies, limitations such as side effects and high recurrence rates persist. Recent research explores alternative therapies, focusing on curcumin's anti-inflammatory, antioxidant, and anti-proliferative properties, which may offer a promising solution for managing uterine fibroid symptoms. This article examines curcumin's therapeutic potential for uterine fibroids, highlighting its benefits and mechanisms.

Keywords

Uterine fibroids; leiomyoma cell; Demethoxycurcumin; Anti-proliferative; Menstrual cramps; Reproductive age; Leiomyoma cells.

Introduction

Pathophysiology of uterine fibroids

Uterine fibroids develop through a complex interplay of molecular mechanisms involving hormones, growth factors, and inflammatory pathways. Estrogen and progesterone stimulate leiomyoma cell

growth, with estrogen inducing progesterone receptor expression and promoting tumor growth. Progesterone regulates growth by modulating various factors, including upregulation of epidermal growth factor (EGF) and B-cell lymphoma 2 (Bcl-2), and downregulation of tumor necrosis factor-alpha (TNF-α) and insulin-like growth factor-1 (IGF-1).

Growth factors such as Transforming Growth Factor-beta (TGF-β) and Platelet-Derived Growth Factor (PDGF) promote cell proliferation and extracellular matrix production. Specifically, TGF-β1 and TGF-β3 promote aberrant survival of leiomyoma cells by downregulating tumor suppressor protein p53 and antagonizing Peroxisome Proliferator-Activated Receptor gamma (PPAR-γ) signaling. The Wingless/Integrated (WNT)/β-catenin, Yes-associated protein (YAP)/Transcriptional Coactivator with PDZ-binding motif (TAZ), and Ras homolog gene family, member A (Rho)/Rho-associated, coiled-coil containing protein kinase (ROCK) pathways also contribute to fibroid formation and development.

Inflammation and impaired antioxidant systems play significant roles in fibroid development, with increased pro-inflammatory cytokines and enzymes contributing to tumor growth. Genetic mutations, including those affecting the Mediator Complex Subunit 12 (MED12) gene, High Mobility Group AT-Hook 2 (HMGA2) overexpression, fumarate hydratase (FH) inactivation, and deletion of collagen genes Collagen Type IV Alpha 5 Chain (COL4A5) and Collagen Type IV Alpha 6 Chain (COL4A6), can also contribute to fibroid development.

Extracellular matrix accumulation and remodeling, mediated by matrix metalloproteinases (MMPs), are essential for fibroid growth and development. The stiffness of the extracellular matrix impacts cell behavior, promoting fibroid growth and symptoms.

Curcumin: the primary bioactive compound

Curcumin, the main polyphenol in turmeric, inhibits uterine fibroid growth and symptoms by reducing cell proliferation, inducing apoptosis, and decreasing extracellular matrix production in leiomyoma cells [1]. Its anti-fibroid activity is attributed to modulating signaling pathways, including Peroxisome Proliferator-Activated Receptor gamma (PPARγ), which regulates cell growth and differentiation [2]. Curcumin stimulates Cysteine-aspartic acid protease-3 (caspase-3) and Cysteine-aspartic acid protease-9 (caspase-9) expression while inhibiting Extracellular Signal-Regulated Kinase 1 (ERK 1), Extracellular Signal-Regulated Kinase 2 (ERK 2), and Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB), suggesting regulation of leiomyocyte apoptosis [3].

Curcumin also inhibits fibronectin production, a key component of the extracellular matrix often overexpressed in leiomyomas, potentially decreasing fibroid size and symptoms [4]. Furthermore, it decreases collagen-1A1 and fibronectin protein expression, essential for extracellular matrix production [5]. Curcumin's antioxidant properties may contribute to anti-fibroid effects by increasing antioxidant enzymes like catalase, superoxide dismutase, and glutathione peroxidase [6].

Clinical studies demonstrate curcumin's efficacy in reducing uterine fibroid size and symptoms. A 6-month study found a significant reduction in fibroid size without adverse effects in patients taking 1.2g of curcumin daily [7]. Another 3-month study reported decreased uterine and myoma volume with increased

hemoglobin percentage in patients taking 1.35g of curcumin daily [8]. However, curcumin's poor bioavailability due to rapid absorption and metabolism may limit its effectiveness [9]. Despite this limitation, curcumin remains a promising natural compound for treating uterine fibroids due to its ability to regulate apoptosis, modulate signaling pathways, and inhibit extracellular matrix production.

Demethoxycurcumin (DMC): anti-inflammatory effects

Demethoxycurcumin (DMC), a curcumin derivative, exhibits potent anti-inflammatory effects that may reduce fibroid symptoms by decreasing inflammation and oxidative stress [5]. DMC significantly decreases extracellular matrix proteins, including collagen-1A1 and fibronectin, which contribute to fibroid growth [4]. Specifically, DMC reduces collagen-1A1 (2.5-fold to 4.14-fold) and fibronectin (1.33-fold to 1.76-fold) protein levels in leiomyoma cells [1].

DMC's anti-inflammatory effects involve modulating key signaling pathways, including AKT (Protein Kinase B) and NF-κB (Nuclear Factor kappa-light-chain-enhancer of activated B cells) pathway inhibition in leiomyoma cells [3]. By regulating inflammation, cell proliferation, and apoptosis, NF-κB inhibition may reduce inflammation and fibroid growth. DMC may also enhance its therapeutic effects by increasing Vitamin D receptor protein expression in leiomyoma cells [1].

Furthermore, DMC's ability to modulate oxidative stress supports its potential therapeutic benefits in reducing fibroid symptoms [6].

Bisdemethoxycurcumin (BDMC): antioxidant and anti-proliferative effects

Bisdemethoxycurcumin (BDMC), a curcumin derivative, exhibits promising antioxidant and anti-proliferative effects that may reduce fibroid growth by inhibiting cell proliferation and inducing apoptosis in leiomyoma cells through modulation of signaling pathways involved in cell growth and differentiation.

BDMC's anti-tumor effects are notable, demonstrated by reduced cell viability and induced apoptosis in human glioblastoma cells through inhibition of B-cell lymphoma 2 (Bcl-2) and increased Bcl-2-associated X protein (Bax) and cytochrome c release. Additionally, BDMC prevents Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway activation in ovarian cancer cells, reducing oxidative stress and matrix metalloproteinase (MMP) expressions.

BDMC's stability, attributed to its resistance to autoxidation, enhances its therapeutic potential. While further research is needed, existing evidence suggests BDMC's value in developing novel therapies. Researchers are exploring methods to improve BDMC's delivery and efficacy, including microfluidic-fabricated thermosensitive liposomes.

Turmerones: sesquiterpenoids with therapeutic potential

Turmerones, sesquiterpenoids in turmeric, show promise in reducing inflammation and oxidative stress, potentially benefiting uterine fibroid treatment. Curcumin, a related compound, exhibits anti-inflammatory and antioxidant effects in reproductive disorders like endometriosis and uterine fibroids by inhibiting Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB) and pro-inflammatory gene expression [2,5,3]. Turmerones may share these mechanisms and enhance curcumin's bioavailability and efficacy. Curcuminoids may also decrease extracellular matrix proteins like collagen-1A1 and fibronectin by inhibiting Protein Kinase B (AKT) activation, contributing to their therapeutic potential [4,5].

Other complementary and alternative remedies for uterine fibroids

Dietary changes, herbal remedies, supplements, and alternative therapies may help alleviate uterine fibroid symptoms. Green tea, rich in antioxidants, has been shown to reduce fibroid growth by inhibiting Catechol-O-Methyltransferase (COMT), an enzyme involved in fibroid pathogenesis [10,11].

Vitamins and nutrients play a crucial role in managing fibroids. Vitamin D supplementation may help prevent and manage fibroids, while vitamin A has been linked to reduce menstrual bleeding. Other beneficial nutrients include B vitamins, vitamin E, beta-carotene, and iron, which can help prevent anemia due to heavy menstrual bleeding.

Herbal remedies with potential benefits include turmeric/curcumin, monk's pepper/chaste berry, blue cohosh, dong quai, wild cherry, astragalus root, and corydalis yanhusuo. These herbs may alleviate symptoms by reducing inflammation, improving blood flow, and balancing hormones. Notably, Guizhi Fuling Formula and Tripterygium wilfordii have shown promise in reducing fibroid volume.

Alternative therapies like acupuncture and mind-body medicine may provide relief. Acupuncture techniques, including electro acupuncture and traditional acupuncture, can shrink fibroids. Additionally, stress reduction techniques like meditation and yoga may alleviate symptoms, while heat therapy can improve blood flow and relax muscles, reducing discomfort.

Conclusion

This review highlights the therapeutic potential of turmeric/curcumin and its bioactive compounds in managing uterine fibroids. Curcumin's anti-inflammatory, antioxidant, and anti-proliferative properties reduce fibroid growth and alleviate symptoms by modulating key signaling pathways, including NF-κB, PPARγ, and AKT. Demethoxycurcumin, bisdemethoxycurcumin, and turmerones also exhibit promising anti-inflammatory and antioxidant effects. Complementary approaches like dietary changes, green tea, vitamin D, and acupuncture may further alleviate symptoms. While further research is needed to determine optimal dosing and efficacy, existing evidence suggests that turmeric/curcumin and its derivatives are valuable adjuncts in uterine fibroid management, offering new avenues for symptom relief and improved outcomes.

About the author

Francis Appiah is a Doctor of Naturopathic Medicine (N.D.) candidate, medical journalist, and medical laboratory technologist, with extensive experience in healthcare administration. With over a decade in Ghana's healthcare sector, he possesses expertise in clinical diagnosis, integrative medicine, patient-centered care, analytical and diagnostic skills, problem-solving, and healthcare management. Guided by his philosophy, "Appiah, F. (2024) To get there, you must be there," he is driven to revolutionize healthcare by bridging conventional and natural medicine for balanced wellness. As the founder of Franapp Mentorship and Wellness Guidance, he empowers individuals to make informed health choices and supports medical professionals. Through Franapp House Call Medicine, he provides comprehensive medical care in patients' homes. His vision is to establish Franapp Holistic Medical Centre. He aims to bridge traditional and holistic healthcare to promote optimal wellness for all Ghanaians.

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