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REVIEW

Standardized Ginkgo Biloba Extract (EGb 761) for Knee Osteoarthritis: A Narrative Review

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Abstract: Knee osteoarthritis (KOA), a prevalent degenerative joint disorder characterized by progressive cartilage degradation, synovial inflammation, and joint dysfunction, remains a major cause of disability worldwide with limited therapeutic options. Ginkgo biloba extract (EGb 761), a standardized multi-component natural product containing flavonoid glycosides and terpene lactones, has demonstrated anti-inflammatory, antioxidant, anti-apoptotic, and Chondroprotection. This narrative review synthesizes current experimental and clinical findings on the potential therapeutic role of EGb 761 in KOA. To provide a comprehensive overview, relevant literature published up to 2025 was identified through searches in PubMed, Scopus, and Web of Science, as well as by screening reference lists of key studies. Considering the complex pathogenesis of KOA and the multi-target pharmacological actions of EGb 761, this review aims to consolidate existing findings and clarify its potential role as an adjunctive therapy. Preclinical and clinical studies suggest that EGb 761 may reduce inflammation, oxidative stress, and chondrocyte apoptosis, leading to modest improvements in pain relief and joint function, while demonstrating a favorable safety profile. However, current evidence is limited by small sample sizes, methodological heterogeneity, short study durations, and risk of bias. While the available evidence is promising, it remains inconclusive that EGb 761 offers significant therapeutic benefits for individuals with KOA. Further high-quality randomized controlled trials are warranted.

Keywords: ginkgo biloba extract, EGb 761, knee osteoarthritis, KOA, efficacy and therapeutic effect

Introduction

Osteoarthritis (OA) is a multifactorial joint disorder primarily affecting weight-bearing joints, characterized by intractable chronic joint pain that significantly impairs patients' mobility and diminishes their quality of life.[1] Among the various subtypes of OA, KOA has emerged as a focal point in clinical research due to its high disability rate.[2] Not only does KOA substantially reduce patients' quality of life, but it also poses a significant global public health challenge exacerbated by the increasing trend of population aging.[3] Furthermore, the disease burden is further complicated by surgical interventions, which while effective for symptom management, present their own set of clinical limitations. Current treatment strategies encompass pharmacological approaches, including intra-articular injections or oral administration of glucocorticoids, paracetamol, or viscoelastic supplements, as well as surgical options such as arthroplasty and tissue engineering.[4,5] However, existing therapies exhibit universal limitations: pharmacological interventions provide only transient symptomatic relief, while prosthetic implants face clinical challenges including their limited service life.[6]

The EGb 761, prepared through a "dual adsorption-elimination" process, represents a promising therapeutic avenue. This formulation is enriched with bioactive components, including flavonoid glycosides and terpene trilactones, which contribute to its multifaceted therapeutic effects. These include lipid metabolism regulation, free radical scavenging, and inflammatory cascade suppression.[7] Recent investigations have underscored the growing therapeutic significance of EGb 761 in diverse domains, ranging from neuroprotection and oxidative stress modulation and oxidative stress modulation to articular inflammation alleviation.[8–10]

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Although EGb 761 has demonstrated therapeutic potential across a variety of diseases,[8] its application in KOA remains in the preliminary stages of investigation. The current body of evidence is limited and heterogeneous, with most studies involving small sample sizes, short follow-up durations, and inconsistent clinical outcomes.[11] Moreover, relatively few studies have explicitly identified the use of the EGb 761, as opposed to non-standardized Ginkgo biloba preparations, which are known to differ substantially in composition, bioactivity, and pharmaceutical quality. This lack of specification may compromise the reliability, reproducibility, and translational relevance of existing findings.[12]

Therefore, this review aims to summarize and critically appraise the current evidence regarding the therapeutic potential of the EGb 761 in KOA, with a particular focus on its anti-inflammatory, anti-oxidant, anti-apoptotic, and chondroprotection mechanisms.

The Epidemiological Characteristics of KOA

OA is a degenerative disease characterized by three core pathological features: progressive destruction of articular cartilage, inflammatory responses in synovial tissue, and structural degeneration of joints. It predominantly affects the weight-bearing joints of the lower extremities that are subject to substantial biomechanical loading.[10,13–15] Metabolic dysregulation of the cartilage matrix, inflammatory imbalance within the synovial microenvironment, and persistent pain constitute its core clinical features. The multifactorial pathogenesis of OA involves aberrant mechanical loading, metabolic dysfunction, and genetic susceptibility.[6,16–18] Key pathological processes include subchondral bone remodeling, excessive secretion of synovial inflammatory mediators, and loss of extracellular matrix (ECM) integrity, ultimately leading to chronic pain and joint dysfunction.[19] KOA, the most prevalent subtype, presents with knee pain, swelling, morning stiffness, and restricted movement.[2] Pain-induced immobility exacerbates muscle atrophy and joint instability, creating a vicious cycle of pain, dysfunction, and progressive structural damage.[18,20–22] In China, KOA accounts for 14.6% of all OA cases. With the aging population, the disease burden associated with KOA is expected to continue increasing.[6,16,23,24] Current management strategies for KOA follow a tiered pharmacologic framework. Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended as first-line therapy for mild-to-moderate symptoms. Refractory cases may require oral analgesics, intra-articular corticosteroids, or other injection therapies for temporary relief.[25–27] When conservative management fails, surgical interventions such as arthroplasty or arthrodesis are performed to restore joint function and alleviate chronic pain.[4]

Despite these strategies, current therapeutic modalities exhibit significant limitations in both symptom alleviation and disease progression retardation.[6,10] Consequently, advancing our understanding of the underlying pathogenesis and developing more efficacious therapeutic approaches have become critical challenges in contemporary medical research.

The Historical Medicinal Value of Ginkgo and Modern Extract Research

Traditional Chinese Medicine (TCM), as a holistic medical system with over two millennia of clinical practice, has demonstrated therapeutic efficacy validated through multiple dimensions.[28] The advancement of modern research technologies has catalyzed the establishment of the TCM Integrated Database (TCMID) and the Systems Pharmacology Platform (TCMSP), providing novel research paradigms for deciphering the molecular targets of herbal formulations.[29] In OA management, TCM has developed distinctive intervention strategies, including bone metabolism regulation using Cornus officinalis,[30] and anti-inflammatory formulations derived from Carthamus tinctorius.[31] Herbal preparations, such as compound formulations containing artificial tiger bone powder and Psammosilene tunicoides components, have shown promise in analgesia and disease progression retardation.[32–34] However, their underlying molecular mechanisms and long-term therapeutic outcomes and safety profiles still require rigorous evidence-based validation through well-designed preclinical and clinical studies.

Ginkgo biloba, a “living fossil” in the plant kingdom, has its medicinal value systematically recorded as early as the Song Dynasty in the “Shennong Bencao Tujing”. Subsequent classic medical texts such as Li Shizhen’s “Compendium of Materia Medica” and Wang Ang’s “Bencao Fengyuan” further refined its clinical application system.[35] As the sole extant representative of the Ginkgoaceae family, Ginkgo biloba’s ecological continuity is attributed to its robust environmental adaptability, pest and disease resistance, as well as close associations with religious/cultural conservation practices.[36] Modern pharmacological research has identified over 60 bioactive compounds in standardized Ginkgo biloba extracts, including flavonoids (approximately 24%) and terpenoid lactones (about 6%), which are considered the primary active

constituents. Additionally, the leaves contain organic acids, proanthocyanidins, tannins, sitosterols, carotenoids, polysaccharides, glucose, minerals, vitamins, and other bioactive compounds.[37] Notably, 10 characteristic diterpene lactones, collectively referred to as ginkgolides (including Ginkgolide A(GA), Ginkgolide B(GB), Ginkgolide C(GC), Ginkgolide J(GJ)) have been isolated and characterized from the terpenoid fraction.[38]

EGb 761, a widely used standardized Ginkgo biloba extract, has been extensively studied for its pharmacological properties. It is derived from Ginkgo leaves and standardized to contain 24% ginkgo-flavone glycosides and 6% terpenoid lactones with the following major constituents (greater than 0.1%):flavonol monoglycosides (eg, quercetin-3-0-glucoside, quercetin-3-0-rhamnoside, and 30-0-methylmyricetin-3-0 glucoside), flavonol diglycosides, flavonol triglycosides, coumaric esters of flavonol diglycosides, flavonoidic compounds, terpenes (eg, BB, GA, GB, GC,GJ), organic acids, and steroids.[39–41] The flavonoid glycosides are primarily composed of quercetin, kaempferol, and isorhamnetin glycosides. The terpene trilactones are primarily composed of bilobalide, Ginkgolides A, B, C, and J.[42] Flavonoid glycosides are the major constituents of EGb 761 and are well known to be an antioxidant for inhibiting tumor growth, also has anti-aging, anti-cancer, anti-inflammatory, anti-microbial, cardioprotective, neuroprotective, and UV-protective effects and so on.[42]

Unlike non-standardized Ginkgo preparations, EGb 761 is manufactured through tightly controlled processes, ensuring batch-to-batch consistency, stability, and safety.[43] Its production involves innovative separation and purification technologies, supported by a stringent quality control system that ensures the purity, stability, and clinical efficacy of its active constituents. These features contribute to its superior safety and therapeutic performance compared to non-standardized extracts.[43] Its pharmacological profile includes potent antioxidant and neuroprotective effects, mediated through free radical scavenging, mitochondrial protection, and modulation of signaling pathways.[44] While EGb 761 has been most thoroughly studied in neurodegenerative disorders such as dementia, Alzheimer's disease, and stroke,[45–50] growing preclinical data support its relevance in OA, which including KOA.[51]

EGb 761 and its main bioactive components—flavonoids and ginkgolides—exert anti-inflammatory, antioxidant, and anti-apoptotic effects through preservation of mitochondrial function[52–55] (Table 1). These mechanisms help protect chondrocytes, reduce synovial inflammation, and preserve ECM integrity.[10,51]

Although clinical trials in KOA are limited, EGb 761 has been safely used for decades, with a well-characterized pharmacological profile. Its pleiotropic properties offer promising therapeutic potential for KOA, warranting further clinical investigation.

The Therapeutic Potential of EGb 761 in KOA

EGb 761 has garnered significant attention due to its mechanisms of action aligning closely with the pathological features of KOA. EGb 761 may attenuate joint degeneration through anti-inflammatory, anti-apoptotic, and antioxidant mechanisms, thereby providing a theoretical foundation for its potential application in the treatment of joint diseases[51,56–58] (Figure 1).

Table 1 The Main Active Ingredients and Functions of EGb 761

Active Ingredient	Action Mechanism	Indications / Efficacy	References
Flavonol glycosides (Quercetin, kaempferol, isorhamnetin)	Anti-oxidant: Scavenges free radicals. Anti-inflammatory: Inhibits NF-κB signaling. Anti-tumor/Anti-aging: Inhibits cellular senescence and tumor proliferation. Reduces inflammatory mediators: Decreases NO and PGE2 levels.	Nervous degenerative diseases (AD, dementia) Osteoarthritis (KOA) Cardiovascular protection	[39–41,52–55]
Terpenoids Ginkgolides A, B, C, J	Inhibition of platelet activating factor (PAF) Anti-inflammatory Improving microcirculation Protect cartilage and inhibit apoptosis	Cerebrovascular disease (stroke) KOA, improve cartilage blood flow Anti-allergy	[42–50]
Bilobalide	Mitochondrial protection Neuroprotection (inhibition of glutamate release) Reduce neurotoxicity	Nervous degenerative diseases OA with neuropathic pain	[42]
Organic acids and steroids	Auxiliary stable extract May be synergistic antioxidant and anti-inflammatory	Improve bioavailability and stability	[39–41]

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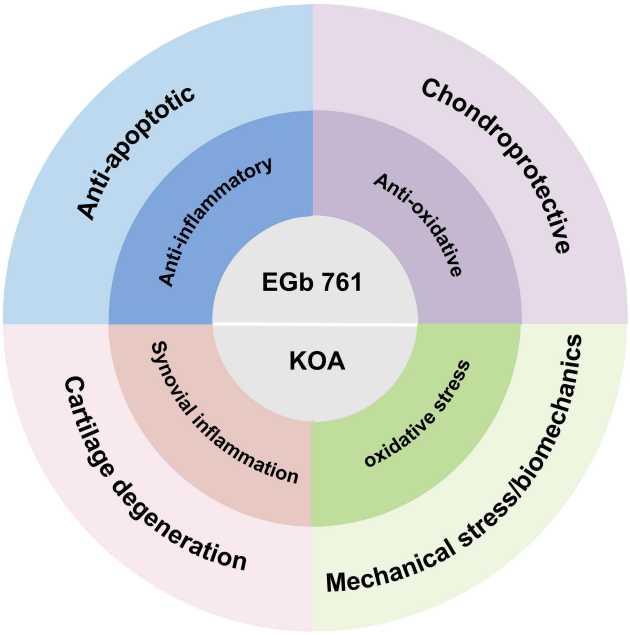

Figure 1 The multiple action mechanisms of EGb 761 in KOA.

Anti-Inflammatory Effect and Anti-Apoptotic Effect

EGb 761 has been shown to inhibit the release of inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and interleukin-1β (IL-1β), thereby alleviating arthritis symptoms, reducing pain and swelling in patients with KOA, and improving joint function.[59,60] Studies have demonstrated that EGb 761 protects chondrocytes from IL-1β-induced damage and significantly downregulates the expression of key inflammatory markers, including inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), and TNF-α.[58,61] EGb 761 not only suppresses the production of inflammatory mediators by downregulating these markers but also modulates immune responses by promoting apoptosis of effector T cells, thereby reducing excessive immune activation and the risk of chronic inflammation.[62]

Moreover, EGb 761 decreases the levels of prostaglandin E2 (PGE2) and nitric oxide (NO) in the bloodstream, attenuates histopathological changes, and inhibits the expression of COX-2 and nitrotyrosine in cartilage, thereby exerting anti-inflammatory effects on both human articular chondrocytes and OA animal models.[10] Additionally, EGb 761 reduces the expression of phosphorylated nuclear factor κB p65 (p-NF-κB p65) and prevents TNF-α-induced activation of the NF-κB pathway in human chondrocytes, which is the mechanism essential for mitigating joint inflammation.[63]

Given the pharmacological profile of EGb 761 and the inflammatory nature of OA pathogenesis, this extract shows strong potential in modulating inflammatory responses in KOA. Together, these findings suggest EGb 761 may modulate both local inflammation and systemic immune activation in KOA.

In addition to its anti-inflammatory role, EGb 761 exhibits anti-apoptotic properties that contribute to cartilage preservation. It attenuates TNF-α-induced apoptosis in osteoarthritic chondrocytes by preserving mitochondrial membrane potential and modulating apoptotic regulators such as increasing Bcl-2 expression and inhibiting caspase-3 activity.[10,64–66] Moreover, EGb 761 reduces the expression of matrix-degrading enzymes including matrix metalloproteinases (MMP-1, MMP-3, and MMP-13), and inhibits type II collagen breakdown, highlighting its anti-catabolic potential in OA.[51]

Anti-Oxidative Stress

Oxidative stress plays a pivotal role in the progression of KOA, contributing to chondrocyte dysfunction, ECM degradation, and mitochondrial impairment.[67] EGb 761 exhibits potent antioxidant activity, as demonstrated in various preclinical models. It enhances endogenous antioxidant defenses by upregulating key enzymes such as superoxide

dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT), which are essential for the neutralization of reactive oxygen species (ROS).[68,69]

In addition, EGb 761 reduces levels of malondialdehyde (MDA) while increasing the activity of glutathione (GSH) and SOD. In erythrocyte models, it counteracts hydrogen peroxide (H_2O_2)-induced oxidative injury by preserving membrane cytoskeletal integrity. In KOA chondrocytes, ROS accumulation contributes to cellular dysfunction, and EGb 761 may exert protective effects via similar antioxidative pathways.[70]

Furthermore, EGb 761 stabilizes mitochondrial membrane potential and attenuates oxidative stress-induced apoptosis. As mitochondrial dysfunction is a major contributor to cartilage degeneration in KOA, EGb 761 may delay chondrocyte death by preserving mitochondrial energy metabolism.[8]

Taken together, these findings support the antioxidative potential of EGb 761 in joint tissues, although most mechanistic data to date derive from preclinical studies. Further investigation is needed to determine whether these antioxidant effects translate into clinical benefits for KOA patients.

Chondroprotection

Though direct data in KOA remain limited, EGb 761 is known neuroprotective actions—such as inhibition of oxidative stress-induced apoptosis and mitochondrial dysfunction—suggest overlapping mechanisms that may be relevant in joint tissues.[64] EGb 761 exerts neuroprotective effects on both sensory and motor neurons following peripheral nerve injury,[71,72] which may contribute to the alleviation of OA-related neuropathic pain and thereby improve patient symptoms. Additionally, EGb 761 has been shown to inhibit glutamate release, potentially reducing neuroexcitotoxicity and indirectly protecting periarticular tissues from excitotoxic damage[73] (Figure 2). These findings support its potential role in delaying cartilage degeneration by targeting shared apoptotic and oxidative stress pathways implicated in KOA progression.

In addition to its neuroprotective actions, EGb 761 exerts direct chondroprotective effects. In an in vitro–in vivo study, EGb 761 significantly attenuated inflammatory responses in human articular chondrocytes stimulated with lipopolysaccharide (LPS) or IL-1β, as evidenced by reductions in PGE_2 and NO production, alongside downregulation

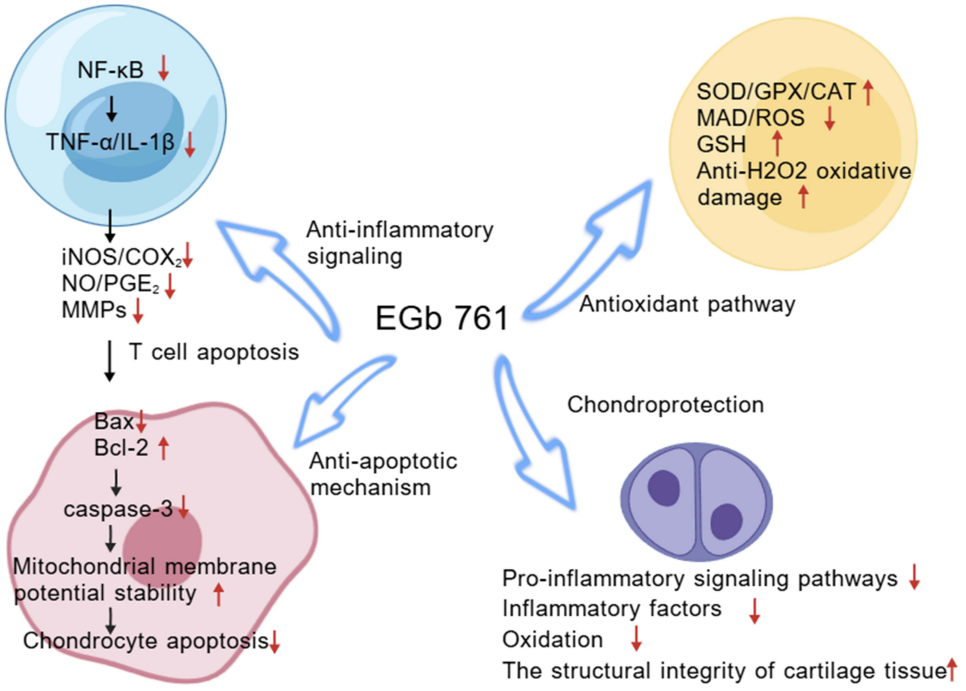

Figure 2 The chondroprotection, antioxidant, anti-apoptotic, and anti-inflammatory mechanisms of EGb 761.Red arrows: Indicating an increase or decrease. Black arrows: Indicating signal pathway direction.

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of COX-2, iNOS, Toll-like receptor 4 (TLR4)/tumor necrosis factor receptor-associated factor 6 (TRAF6), and nuclear factor-κB (NF-κB) signaling. Consistently, in a rat model of OA, systemic administration of EGb 761 led to decreased circulating levels of PGE_2 and NO, improved cartilage histopathological scores, and reduced COX-2 and nitrotyrosine immunoreactivity in joint tissues. These findings suggest that EGb 761 protects cartilage by modulating pro-inflammatory mediators and preserving structural integrity in the osteoarthritic joint.[10,58]

Safety and Drug Interactions

EGb 761 is generally regarded as safe and well-tolerated when administered at recommended therapeutic doses. Its safety profile is supported by decades of clinical use and extensive pharmacovigilance data. Reported adverse effects are typically mild and transient, including gastrointestinal discomfort, headache, dizziness, skin allergies, elevated blood pressure, and occasional respiratory tract infections.[74] Most adverse events have been documented in case reports involving doses ranging from 80 to 150 mg/day for treatment durations spanning from one week to one year, often in patients with comorbidities or those concurrently using other medications.[41]

Notably, several case studies have raised concerns regarding bleeding abnormalities potentially associated with Ginkgo biloba, including postoperative hemorrhage and increased bleeding risk during anticoagulant therapy[75] These effects are thought to be mediated by ginkgolides and bilobalide—constituents of EGb 761—which function as Platelet-Activating Factor (PAF) receptor antagonists. Although the absolute risk remains low, clinicians should exercise caution when EGb 761 is used concomitantly with anticoagulants (eg, warfarin), antiplatelet agents (eg, aspirin, clopidogrel), or nonsteroidal NSAIDs, especially in elderly individuals or those undergoing surgical procedures.[76]

Conclusion

KOA is a multifactorial degenerative disease with complex pathogenesis involving inflammation, oxidative stress, chondrocyte apoptosis, and ECM degradation. Current treatment strategies remain limited, prompting the search for novel adjunctive therapies. EGb 761, exhibits multiple pharmacological activities—including anti-inflammatory, anti-oxidant, anti-apoptotic, and chondroprotective effects—supported by extensive preclinical research.[59,60]

However, the clinical evidence for EGb 761 in KOA remains limited. Only a small number of randomized trials have been conducted, with small sample sizes, variable designs, short follow-up durations, and inconsistent outcome measures. Most mechanistic insights stem from in vitro or animal models, and their translation into clinical benefit is not yet established. While safety data appear generally favorable, they are mostly derived from non-OA populations, and long-term safety in OA patients remains insufficiently characterized.[75]

Therefore, EGb 761 should not yet be considered a practice-changing intervention for KOA. Instead, it represents a hypothesis-generating candidate that warrants further investigation. Future studies should employ standardized EGb 761 formulations, include adequately powered randomized controlled trials with prespecified pain and functional outcomes, long-term follow-up, and systematic safety reporting—including drug interaction monitoring—especially in elderly OA populations. A more robust evidence base is required before EGb 761 can be recommended for routine use in KOA management.

Abbreviations

KOA, Knee osteoarthritis; EGb 761, Ginkgo biloba extract; OA, Osteoarthritis; ECM, Extracellular Matrix; NSAIDs, Nonsteroidal anti-inflammatory drugs; TCM, Traditional Chinese Medicine; TCMID, TCM Integrated Database; TCMSP, TCM Systems Pharmacology Platform; BB, Bilobalide; GA, Ginkgolide A; GB, Ginkgolide B; GC, Ginkgolide C; GK, Ginkgolide K; GJ, Ginkgolide J; TNF-α, Tumor Necrosis Factor-alpha; IL-1β, Interleukin-1β; iNOS, Inducible Nitric Oxide Synthase; PGE2, Prostaglandin E2; COX-2, Cyclooxygenase-2; NO, nitric oxide; P-NF-KB P65, Phosphorylated Nuclear Factor KB P65; MMps, Matrix Metalloproteinases; SOD, Superoxide Dismutase; Gpx, Glutathione Peroxidase; CAT, Catalase; ROS, Reactive Oxygen Species; MDA, Malondialdehyde; GSH, Glutathione; H_2O_2, hydrogen peroxide; LPS, Lipopolysaccharide; TLR4, tumor Toll-like receptor 4; TRAF6, necrosis factor receptor-associated factor 6; NF-κB, nuclear factor-κB; PAF, Platelet-Activating Factor.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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