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MINI REVIEW

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Boswellic acids in liver health: Potential against Non-Alcoholic Fatty Liver Disease (NAFLD)

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ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disorder globally, with limited pharmacological treatment options. Recent scientific interest has turned to natural compounds with multi-targeted effects, such as Boswellic acids (BAs), derived from the gum resin of Boswellia species. BAs, particularly acetyl-11-keto-β-boswellic acid (AKBA), exhibit potent anti-inflammatory and antioxidant properties, making them promising candidates for hepatoprotection. This mini-review explores the mechanistic role of BAs in managing NAFLD and highlights key findings from preclinical studies. BAs mitigate NAFLD progression by inhibiting inflammatory pathways like NF-κB and 5-lipoxygenase (5-LOX), enhancing antioxidant defense via Nrf2 activation, and modulating lipid metabolism. In animal models, BA supplementation has led to reductions in hepatic steatosis, fibrosis, and serum liver enzymes. Despite limited clinical data in NAFLD patients, BAs have demonstrated liver function benefits and safety in trials on other chronic inflammatory diseases. However, challenges such as low bioavailability, lack of standardization, and insufficient human trials hinder their clinical adoption. Future directions include advanced delivery systems and well-designed clinical studies. Overall, Boswellic acids hold significant potential as nutraceutical agents in liver health and warrant further exploration in NAFLD therapy.

KEYWORDS

Antioxidants; Frankincense; Boswellia; Metabolic syndrome; Insulin resistance; Global health; Sedentary behavior

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Introduction

Non-alcoholic fatty liver disease (NAFLD) represents a rapidly increasing global health concern and is currently the most prevalent liver disorder worldwide [1]. It encompasses a spectrum of hepatic abnormalities, including simple steatosis (fat accumulation in liver cells), non-alcoholic steatohepatitis (NASH) characterized by hepatic inflammation and cell damage, and advanced stages such as fibrosis, cirrhosis, and hepatocellular carcinoma. NAFLD is commonly associated with obesity, insulin resistance, metabolic syndrome, and sedentary lifestyles. Alarmingly, its incidence is rising even among children and adolescents.

In this context, there is growing interest in nutraceuticals, bioactive compounds from natural sources with health benefits as potential adjuncts or alternatives to conventional therapies. Boswellic acids (BAs), derived from the resin of the Boswellia species (commonly known as frankincense), have garnered attention for their potent anti-inflammatory, antioxidant, and anti-fibrotic effects [2]. These pharmacological properties are particularly relevant to the multifactorial pathogenesis of NAFLD. This mini-review explores the potential of BAs as therapeutic agents in managing NAFLD, highlighting their mechanisms of action, preclinical and clinical evidence, and the challenges that must be addressed to translate these findings into clinical practice.

Boswellic Acids: Source and Chemistry

Boswellic acids are a class of pentacyclic triterpenoids extracted from the oleo-gum resin of trees belonging to the genus Boswellia, particularly Boswellia serrata, Boswellia carterii, and Boswellia sacra. These trees are native to regions of India, North Africa, and the Middle East. The resin has been used in traditional medicine for centuries to treat inflammatory conditions, particularly in Ayurvedic and Unani systems [3].

The pharmacologically significant boswellic acids include β-boswellic acid (BA), acetyl-β-boswellic acid (ABA), 11-keto-β-boswellic acid (KBA), and acetyl-11-keto-β-boswellic acid (AKBA). Among these, AKBA is considered the most bioactive due to its potent inhibitory effect on 5-lipoxygenase (5-LOX), an enzyme pivotal in the biosynthesis of leukotrienes involved in inflammation [4]. Boswellic acids also modulate nuclear factor-kappa B (NF-κB), a transcription factor that regulates the expression of genes linked to chronic inflammation. The unique chemical structure of boswellic acids, characterized by carboxylic and keto functional groups, is key to their biological activity.

Pathophysiology of NAFLD

The development and progression of NAFLD are multifactorial, involving complex interactions between metabolic, oxidative, inflammatory, and fibrotic processes [5]. The most widely accepted model explaining its pathogenesis is the "multiple-hit hypothesis," which includes insulin resistance, lipid accumulation, oxidative stress, mitochondrial dysfunction, and chronic inflammation as key contributors.

Insulin resistance leads to increased lipolysis in adipose tissue, resulting in elevated free fatty acid levels in the

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bloodstream that accumulate in hepatocytes. This triggers mitochondrial dysfunction and increased production of reactive oxygen species (ROS), causing lipid peroxidation, DNA damage, and hepatocellular injury. Subsequently, immune responses and the release of pro-inflammatory cytokines like TNF-α and IL-6 exacerbate hepatic inflammation. Persistent inflammation activates hepatic stellate cells (HSCs), which transform into myofibroblasts and produce excessive extracellular matrix proteins, contributing to liver fibrosis [6]. Thus, a successful therapeutic agent must address multiple pathological pathways to be effective in NAFLD management.

Mechanisms of Action of Boswellic Acids in Liver Protection

Boswellic acids exert multiple pharmacological actions that are beneficial in preventing or attenuating the progression of NAFLD.

Anti-inflammatory effects

BAs inhibit 5-lipoxygenase (5-LOX), thereby reducing the synthesis of pro-inflammatory leukotrienes. Additionally, BAs suppress the activation of nuclear factor-kappa B (NF-κB), which regulates the expression of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. These actions collectively reduce the hepatic inflammatory response, a critical driver of NASH and fibrosis [7].

Antioxidant properties

BAs enhance the body's antioxidant defense mechanisms by activating nuclear factor erythroid 2 related factor 2 (Nrf2), a transcription factor that stimulates the expression of antioxidant enzymes including glutathione peroxidase, catalase, and superoxide dismutase. This reduces oxidative stress and lipid peroxidation, protecting liver cells from further damage.

Regulation of lipid metabolism

BAs have been shown to downregulate lipogenic genes such as sterol regulatory element-binding protein-1c (SREBP-1c) and fatty acid synthase (FAS), which are involved in hepatic fat synthesis. Concurrently, BAs may promote fatty acid oxidation through upregulation of peroxisome proliferator-activated receptor alpha (PPAR-α), thereby reducing triglyceride accumulation in the liver [8].

Anti-fibrotic action

BAs inhibit the profibrotic cytokine transforming growth factor-beta (TGF-β), a major activator of hepatic stellate cells. This reduces the expression of fibrotic markers such as alpha-smooth muscle actin (α-SMA) and collagen type I, slowing the progression of liver fibrosis.

Preclinical Studies Supporting Boswellic Acids in NAFLD

A growing body of preclinical research provides compelling evidence for the therapeutic potential of boswellic acids (BAs) in the management of non-alcoholic fatty liver disease (NAFLD). In various animal models of NAFLD, typically induced by high-fat diets (HFD), fructose feeding, or chemical hepatotoxins, BAs have demonstrated significant hepatoprotective effects. For instance, in HFD-induced obese rats, BA supplementation led to marked reductions in hepatic triglyceride content, normalization of liver enzyme levels (ALT and AST), and improvement in histopathological features such as steatosis and ballooning degeneration. Studies have shown that these improvements are closely linked to BAs' ability to inhibit key inflammatory mediators (e.g., TNF-α, IL-1β), reduce oxidative stress via upregulation of endogenous antioxidant enzymes, and modulate lipid metabolism through pathways involving SREBP-1c and PPAR-α. Additionally, in chemically induced liver fibrosis models (e.g., carbon tetrachloride or thioacetamide), BAs suppressed hepatic stellate cell activation, reduced collagen deposition, and downregulated fibrogenic markers such as TGF-β1 and α-SMA [9]. Notably, some studies also reported enhanced insulin sensitivity and improved glucose metabolism in BA-treated groups. These findings collectively support the multifaceted mechanisms through which boswellic acids may counteract the pathogenesis of NAFLD, warranting further translational and clinical investigations.

Clinical Evidence and Safety

Although direct clinical evidence on the efficacy of boswellic acids (BAs) in managing non-alcoholic fatty liver disease (NAFLD) is currently limited, insights from related clinical conditions offer promising implications. BAs have been extensively studied in patients with chronic inflammatory disorders such as rheumatoid arthritis, osteoarthritis, asthma, and inflammatory bowel diseases conditions with overlapping pathological features, including systemic inflammation and oxidative stress. These studies consistently demonstrate that BAs, particularly those standardized to high concentrations of acetyl-11-keto-β-boswellic acid (AKBA), reduce levels of pro-inflammatory cytokines like TNF-α and IL-6, modulate oxidative stress markers, and improve overall clinical outcomes. In the context of metabolic syndrome and type 2 diabetes, both closely linked to NAFLD, preliminary findings suggest that BAs may improve insulin sensitivity and lower liver enzyme levels (ALT, AST), indicating potential hepatoprotective effects. Importantly, BAs are generally well-tolerated in human trials, with minimal and self-limiting side effects such as gastrointestinal discomfort or mild rash. Doses ranging from 300 to 1000 mg per day have shown a favorable safety profile [10]. These observations underscore the urgent need for targeted clinical trials assessing BAs in NAFLD populations, where their anti-inflammatory, antioxidant, and lipid-modulating properties could offer a safe and effective adjunct to current therapeutic strategies.

Challenges and Future Directions

Bioavailability

One of the primary challenges limiting the clinical translation of boswellic acids (BAs), particularly acetyl-11-keto-β-boswellic acid (AKBA), is their inherently low oral bioavailability. This limitation stems from poor aqueous solubility, low gastrointestinal permeability, and extensive first-pass metabolism. To overcome this, advanced drug delivery systems are under investigation. These include nanoformulations, liposomes, solid lipid nanoparticles, and phytosomes, all of which aim to improve dissolution, absorption, and targeted

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delivery. Additionally, co-administration with dietary fats or lipophilic carriers has enhanced systemic absorption and may be strategically employed in future formulation approaches [11].

Product standardization

Another significant barrier to clinical application is the lack of standardized BA formulations. Extracts derived from different Boswellia species, geographic regions, and manufacturing processes often vary widely in their composition and concentration of active boswellic acids, especially AKBA. This variability makes it difficult to ensure reproducibility, compare study outcomes, or establish dosing guidelines. Therefore, rigorous standardization protocols and quality control measures are essential to produce pharmaceutically reliable BA preparations suitable for therapeutic use in NAFLD.

Clinical trials

Although preclinical evidence supports the hepatoprotective role of BAs, there remains a critical gap in high-quality, randomized controlled clinical trials specifically targeting NAFLD. Most human studies to date have focused on inflammatory conditions or metabolic syndrome, offering indirect insights. Future trials must be carefully designed to assess efficacy, safety, dosing regimens, and treatment duration in NAFLD patients, using standardized biomarkers and liver imaging modalities. Such trials are essential to substantiate the therapeutic claims and facilitate regulatory approval.

Synergistic therapies

An emerging and promising area involves the combination of BAs with other nutraceuticals or hepatoprotective agents to enhance efficacy and reduce the required dosage of each component. Co-administration with compounds such as curcumin, silymarin, or omega-3 fatty acids may exert synergistic effects by targeting multiple pathogenic pathways in NAFLD, including oxidative stress, lipid metabolism, and inflammation [12]. These combinations could potentially improve therapeutic outcomes while minimizing side effects. Further mechanistic and clinical studies are needed to optimize such integrative strategies and evaluate their long-term benefits in liver health.

Conclusions

Non-alcoholic fatty liver disease (NAFLD) is a growing global health burden with limited effective pharmacological treatments currently available. In this context, boswellic acids (BAs), particularly acetyl-11-keto-β-boswellic acid (AKBA), offer a promising natural therapeutic approach due to their potent anti-inflammatory, antioxidant, lipid-modulating, and anti-fibrotic properties. Preclinical studies have consistently demonstrated the protective effects of BAs against hepatic steatosis, inflammation, and fibrosis, aligning well with the multifactorial pathogenesis of NAFLD. Although direct clinical trials are still limited, early evidence from related metabolic and inflammatory conditions indicates a favorable safety profile and therapeutic promise.

However, challenges such as low bioavailability, lack of standardized extracts, and the need for robust human trials remain significant barriers to clinical translation. Addressing these gaps through formulation innovations, well-designed clinical studies, and integrative therapeutic approaches may unlock the full potential of BAs as adjunctive agents in NAFLD management. As interest in nutraceuticals continues to rise, boswellic acids represent a compelling candidate for future liver health interventions, potentially bridging the gap between traditional herbal remedies and evidence-based modern medicine.

Disclosure Statement

No potential conflict of interest was reported by the authors.

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