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HEPATOPROTECTIVE EFFECTS OF CURCUMIN IN NON-ALCOHOLIC FATTY LIVER DISEASE: MECHANISMS AND CLINICAL EVIDENCE

EFEITOS HEPATOPROTETORES DA CURCUMINA NA DOENÇA HEPÁTICA GORDUROSA NÃO ALCOÓLICA: MECANISMOS E EVIDÊNCIAS CLÍNICAS

EFECTOS HEPATOPROTECTORES DE LA CURCUMINA EN LA ENFERMEDAD DEL HÍGADO GRASO NO ALCOHÓLICO: MECANISMOS Y EVIDENCIA CLÍNICA

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ABSTRACT

Curcumin, the primary bioactive compound of Curcuma longa, exhibits anti-inflammatory and antioxidant properties with therapeutic potential in non-alcoholic fatty liver disease (NAFLD). This article reviews its mechanisms of action and clinical evidence as a hepatoprotective agent. Curcumin modulates inflammatory pathways by suppressing pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) and activating pathways such as TLR4/NF-κB and AMPK, reducing oxidative stress and hepatic inflammation. Studies indicate that curcumin supplementation improves metabolic parameters, including waist circumference and triglycerides, while also reducing liver fibrosis. However, its effect on liver enzymes is variable, and its low bioavailability limits clinical efficacy. Curcumin demonstrates promising hepatoprotective effects in NAFLD, primarily through the modulation of inflammation and lipid metabolism. Nevertheless, further research is needed to overcome challenges such as bioavailability and to establish optimized therapeutic protocols.

Keywords: Curcumin. NAFLD. Hepatoprotection. Inflammation. Oxidative Stress.

RESUMO

A curcumina, principal composto bioativo da Curcuma longa, apresenta propriedades anti-inflamatórias e antioxidantes com potencial terapêutico na doença hepática gordurosa não alcoólica (DHGNA). Este artigo revisa seus mecanismos de ação e evidências clínicas como agente hepatoprotetor. A curcumina modula vias inflamatórias suprimindo citocinas pró-

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inflamatórias (IL-1β, IL-6, TNF-α) e ativando vias como TLR4/NF-κB e AMPK, reduzindo o estresse oxidativo e a inflamação hepática. Estudos indicam que a suplementação com curcumina melhora parâmetros metabólicos, incluindo circunferência abdominal e triglicerídeos, além de reduzir a fibrose hepática. No entanto, seu efeito sobre as enzimas hepáticas é variável e sua baixa biodisponibilidade limita a eficácia clínica. A curcumina demonstra efeitos hepatoprotetores promissores na DHGNA, principalmente por meio da modulação da inflamação e do metabolismo lipídico. Contudo, mais pesquisas são necessárias para superar desafios como a biodisponibilidade e para estabelecer protocolos terapêuticos otimizados.

Palavras-chave: Curcumina. DHGNA. Hepatoproteção. Inflamação. Estresse Oxidativo.

RESUMEN
La curcumina, el principal compuesto bioactivo de la Curcuma longa, exhibe propiedades antiinflamatorias y antioxidantes con potencial terapéutico en la enfermedad del hígado graso no alcohólico (EHGNA). Este artículo revisa sus mecanismos de acción y la evidencia clínica como agente hepatoprotector. La curcumina modula las vías inflamatorias al suprimir las citocinas proinflamatorias (IL-1β, IL-6, TNF-α) y activar vías como TLR4/NF-κB y AMPK, reduciendo el estrés oxidativo y la inflamación hepática. Los estudios indican que la suplementación con curcumina mejora los parámetros metabólicos, como la circunferencia de la cintura y los triglicéridos, a la vez que reduce la fibrosis hepática. Sin embargo, su efecto sobre las enzimas hepáticas es variable y su baja biodisponibilidad limita su eficacia clínica. La curcumina demuestra prometedores efectos hepatoprotectores en la EHGNA, principalmente a través de la modulación de la inflamación y el metabolismo lipídico. Sin embargo, se necesita más investigación para superar desafíos como la biodisponibilidad y establecer protocolos terapéuticos optimizados.

Palabras clave: Curcumina. EHGNA. Hepatoprotección. Inflamación. Estrés Oxidativo.

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1 INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a metabolic condition characterized by the excessive accumulation of fat in the liver, in the absence of significant alcohol consumption. Its global prevalence has been increasing in parallel with the epidemic of obesity and diabetes, affecting around 25% of the world's population, with potential progression to non-alcoholic steatohepatitis (NASH), liver fibrosis and cirrhosis (Younossi et al., 2018). The pathophysiology of NAFLD involves insulin resistance, oxidative stress and chronic inflammation, making therapeutic strategies that modulate these processes promising targets for intervention (Friedman et al., 2018)

Curcumin, the main bioactive polyphenol in turmeric (Curcuma longa), has attracted attention due to its anti-inflammatory, antioxidant and lipid metabolism modulating properties (Hewlings; Kalman, 2017) Preclinical studies show that curcumin inhibits pro-inflammatory pathways such as NF-κB and TLR4, reduces cytokine production (TNF-α, IL-6) and attenuates oxidative stress by activating the AMPK pathway (Qiu et al., 2023). In addition, clinical trials suggest that its supplementation can improve metabolic parameters, such as reducing liver fat, decreasing liver enzymes (ALT/AST) and attenuating fibrosis (Ranneh et al., 2024; Saadati et al., 2019a)

However, challenges remain, mainly due to the low bioavailability of curcumin, which limits its therapeutic effects in humans (Anand et al., 2007). Strategies such as the use of nanoparticles, adjuvants (piperine) or synthetic analogues have been investigated to overcome this limitation (Kazmi et al., 2022). In addition, clinical results are still heterogeneous, with some studies failing to demonstrate significant benefits on markers of inflammation or fibrosis (Chashmniam et al., 2019).

Given this context, this study aims to critically review the hepatoprotective mechanisms of curcumin in NAFLD and the available clinical evidence, highlighting both its potential and its limitations. The synthesis of this information can guide future research and therapeutic applications, contributing to the development of more effective strategies in the management of NAFLD.

2 METHODOLOGIES

This is an integrative literature review, following a descriptive and analytical approach. The methodology adopted included the selection of articles published in sources such as Pubmed, Scielo and Lilacs. The inclusion criteria were original articles, randomized clinical

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trials and clinical trials published in the last 10 years (2015-2025). Human studies evaluating the effects of curcumin on NAFLD, with a focus on anti-inflammatory mechanisms, antioxidants and clinical parameters (liver enzymes, fibrosis markers, lipid profile). The search strategy used the keywords: “curcumin”, “NAFLD”, “non-alcoholic fatty liver disease”, “hepatoprotection”, “inflammation”, “oxidative stress” and the Boolean operators AND (for intersecting terms) and OR (for synonyms).

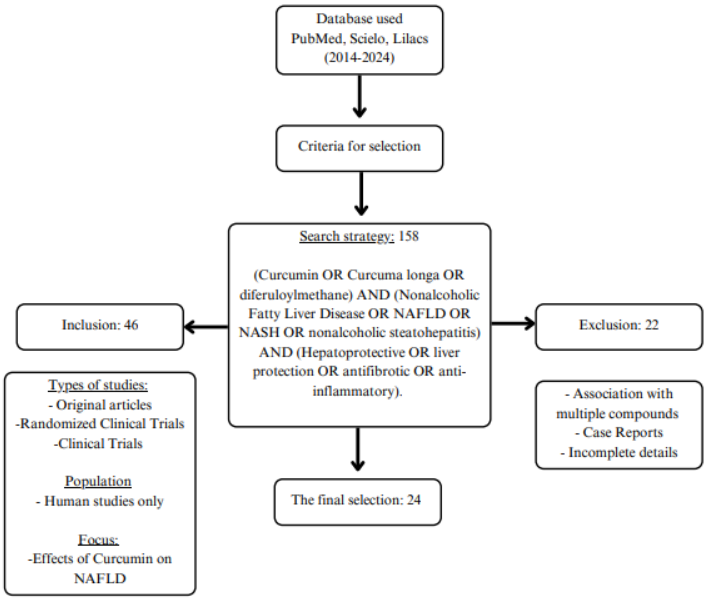
The methodology was structured in four main stages according to the PICO anagram: Population: Patients with NAFLD or experimental models of the disease; Intervention: Supplementation with curcumin or derivatives; Comparison: Placebo or conventional treatment and Outcomes: Markers of inflammation, oxidative stress and liver fibrosis.

The search terms (MeSH) were: (Curcumin OR Curcuma longa OR diferuloylmethane) AND (Nonalcoholic Fatty Liver Disease OR NAFLD OR NASH OR nonalcoholic steatohepatitis) AND (Hepatoprotective OR liver protection OR antifibrotic OR anti-inflammatory). Articles with an association of multiple compounds, case reports and studies with incomplete data on liver parameters were excluded.

After applying the inclusion and exclusion criteria, 24 studies were selected for analysis (Figure 1).

Figure 1

Study organization chart



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These studies were systematically evaluated in terms of their methodological design, study population, supplementation protocols (including dosage and duration), main biochemical and histological findings, as well as the methodological limitations reported by the authors. A comprehensive summary of these results is presented in Table 1, which organizes the data extracted from the selected literature in a comparative manner.

3 RESULTS AND DISCUSSION

The aim of this study was to critically review the mechanisms by which curcumin exerts hepatoprotective effects in non-alcoholic fatty liver disease (NAFLD), analyzing the clinical evidence available in the literature. We sought to evaluate both the therapeutic potential of this natural compound - including its antioxidant, anti-inflammatory and lipid metabolism modulating effects - and its main limitations, such as issues related to bioavailability, variations in clinical responses and the need for more standardized therapeutic protocols. Through this comprehensive analysis, we aimed to offer a balanced view of the current role and future prospects of curcumin in the management of NAFLD.

Table 1 presents the main findings on the hepatoprotective effects of curcumin in NAFLD/NASH (Ashraf; Rather; Mehraj, 2025; Cerletti et al., 2020; Cicero et al., 2020; Hariri et al., 2020; He et al., 2024; Hemati et al., 2025; Jazayeri-Tehrani et al., 2017; Mirhafez et al., 2021c, 2019, 2021b, 2021a; Moradi Kelardeh et al., 2020; Naseri et al., 2022; Saberi-Karimian et al., 2020; Sharifi et al., 2023)

Table 1

Main studies on the hepatoprotective effects of curcumin in NAFLD/NASH

N	Author (year)	Study Design	Population/ Model	Intervention (Dose/Duration)	Main Findings	Limitations	Conclusion
1	(Saadati et al., 2019b)	Randomized, double-blind, placebo-controlled clinical trial	50 adult NAFLD patients	Curcumin (1.5g/day) + Piperine vs Placebo (12 weeks) Cointervention: Balanced diet and physical exercise (> 30 min, 3x/week)	ALT (-22.3%) and AST (-18.7%) in both groups (p<0,001) Improvement in hepatic steatosis (p<0,05)	Small sample; insufficient time; no histological evaluation	Curcumin was not superior to placebo in improving inflammation or fibrosis with NAFLD

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					Reduction in TNF-alpha (p<0,001) and NF-kB (p=0,044) in the curcumin group (no statistical difference)		
2	(Mirhafez et al., 2021c)	Randomized, double-blind clinical trial	45 NAFLD patients (22 curcumin, 22 placebo)	Dose 250 mg/day. 8 weeks.	Reduction in markers of oxidative stress and DNA damage (CML (-25%, P=0.04)) and 8-OHdG (-10%, P=0.03)); Improvement in liver enzymes ALT/AST (p<0.001)	Small sample, insufficient time, low dose of curcumin, lack of histological evaluation, non-standardized diet and exercise	Reduction in oxidative stress, improvement in liver enzymes, improvement in anthropometric parameters
3	(Musso et al., 2025)	Randomized double-blind study	52 patients with NASH	Curcumin (2g) or placebo for 72 weeks	Curcumin group, 50% improvement in liver fibrosis	Small sample, patients with comorbidities	Resolution of NASH and regression of fibrosis
4	(Panahi et al., 2019)	Randomized, double-blind clinical trial	70 patients with NAFLD	Curcuminoids (500 mg/day) + piperine (5mg/day); 12 weeks	Improvement in liver enzymes ALT (p=0.0035) AST (p=0.042) alkaline phosphatase (p=0.004) improvement in lipid profile, reduction in inflammatory markers	Ultrasound evaluation (less precise method), insufficient time (12 weeks); no markers of oxidative stress or inflammation were measured	Reduced liver enzymes and improved lipid profile; reduced inflammatory markers
5	(Rahmani et al., 2016)	Randomized, double-blind clinical trial	80 patients with NAFLD (ultrasound)	Curcumin (500 mg/day), 8 weeks	78.9% reduction in liver fat, metabolic and hepatic improvement	Ultrasound evaluation (less accurate) low dose, lack of markers	Reduced hepatic steatosis, improved metabolism

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6	(Naseri et al., 2022)	Randomized clinical trial	52 patients with NAFLD	Curcumin 1.5 g/day; 12 weeks; lifestyle modification	Reduction in triglycerides/glucose in both groups; reduction in NAFLD (p=0.021) and metabolic syndrome (p=0.012). There was no significant difference in atherogenic indices, adiposity markers and liver indices	Secondary data; Small sample, insufficient time, lack of histological data, dominant effect of lifestyle modification	Curcumin (1.5g/day) did not show significant benefits in NAFLD
7	(Panahi et al., 2017)	Randomized, double-blind clinical trial	102 patients with NAFLD	curcumin (1g/day), 8 weeks + lifestyle advice	Anthropometric improvement (p=0.024), AST/ALT improvement (p<0.001)	Insufficient time, Ultrasound evaluation (less accurate), lack of dietary standardization	Significant improvement in ultrasound parameters of hepatic steatosis; reduction in liver enzymes and anthropometric measurements
8	(Mirhafez et al., 2021b)	Randomized, double-blind clinical trial	79 adults (18-65 years) with NAFLD	Curcumin (500 mg) + piperine (dose not specified), 8 weeks + dietary and exercise advice	Reduction in alkaline phosphatase (-16.2 mg/dL vs -6.0 mg/dL) (p=0.04), improvement in the severity of NAFLD (p=0.04), AST/ALT not reported, anthropometric	Insufficient time, Ultrasound evaluation (less accurate), small sample, small dose	Reduction in alkaline phosphatase, improvement in NAFLD

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					parameters with no statistical difference		
9	(Mirhafez et al., 2021c)	Randomized, double-blind clinical trial	80 adult patients with NAFLD and overweight/obesity	Curcumin phospholipid (250 mg/day), 8 weeks	Reduction in steatosis and AST; improvement in HDL and anthropometric parameters	Low dose, short duration, lack of data on inflammatory markers and oxidative stress	Positive effects on the reduction of hepatic steatosis, improvement in AST
10	(Panahi et al., 2016)	Randomized, double-blind clinical trial	102 adult patients with NAFLD, 8 weeks	Curcumin (1g/day)	Reduction of LDL, TG, uric acid, no effect on glycemia or HDL	Insufficient time, less accurate ultrasound, lack of inflammatory markers	Significant reduction in serum lipids (LDL, triglycerides) and uric acid, with no effect on glycemic parameters (glucose, HbA1c)
11	(Cerletti et al., 2020)	Randomized, double-blind, multicentre clinical trial with two parallel groups	113 subjects (men and women) aged between 18 and 80 diagnosed with NAFLD	Daily supplementation for 3 months with a mixture of DHA, phosphatidylcholine, silymarin, choline, curcumin and vitamin E	Reduction in AST, ALT and GGT) after treatment, with statistical significance only for AST. Metabolic and inflammatory variables remained unchanged, except for a slight increase (<10%) in cholesterol and glucose levels in the active group	Small sample size, limited duration and no significant differences between the groups, suggesting a possible placebo effect or the need for a longer intervention time.	Chronic supplementation was well tolerated and safe. No significant efficacy in the pathophysiological markers evaluated.
12	(Saberi-Karimian	Randomized, double-	55 patients with NAFLD	Curcumin (500 mg) + Piperine	Weight reduction (p=0.016),	Small sample, not enough time	Reduction of inflammatory markers

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	et al., 2020)	blind clinical trial		(5 mg), 8 weeks	improvement in NAFLD (p=0.002), reduction in inflammatory markers TNF-alpha (p=0.024), MCP-1 (p=0.008) and EGF (p=0.0001).		(TNF-α, MCP-1, EGF), better ultrasound parameters of NAFLD and significant weight reduction
13	(Jazayeri-Tehrani et al., 2017)	Randomized, double-blind clinical trial	84 obese patients (BMI>30 kg.m2) with NAFLD + lifestyle counseling	Nanocurcumin 80mg/day; duration 3 months, monthly follow-up		Low dose, less accurate ultrasound, co-intervention bias	
14	(Hariri et al., 2020)	Randomized, double-blind clinical trial	54 patients with NAFLD	250 mg/day, 8 weeks	Significant reduction in methylation of the promoter regions of the MLH1 and MSH2 genes in the curcumin group, ALT/AST no difference between groups	Small sample (44 completed the study), short duration, low dose (250 mg/day), few genes evaluated	Curcumin modulated genes in NAFLD, but did not affect liver damage.
15	(Hemati et al., 2025)	Triple-blind, randomized clinical trial	44 women with ER+ breast cancer, using tamoxifen, curcumin group vs placebo	Curcumin 500 mg/day, 6 months	Increase in degree of NAFLD 13.6% (curcumin) vs 54.5% (placebo) p=0.03	Small sample size, moderate duration, ultrasound evaluation (less sensitive than biopsy or MRI), Specific population (CA breast ER+)	Curcumin prevented NAFLD caused by tamoxifen in breast cancer without side effects, but requires a larger n for validation.

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16	(Moradi Kelardeh et al., 2020)	Randomized, controlled, 4-arm clinical trial	5 elderly and obese women with NAFLD, 12 weeks	Resistance exercises; Curcumin (not specified), placebo (P and RT)	Improved liver function (RT and RTC), reduced ALT/AST (p=0.05)	Small sample, short duration, unspecified dose, ultrasound evaluation	Improved liver function (AST/ALT), synergistic effect with physical exercise
17	(Cicero et al., 2020)	Randomized, double-blind clinical trial	80 overweight individuals	Curcumin (800 mg/day), 8 weeks	Reduction in fasting glucose, insulin, HOMA-IR, trig, AST/ALT, cortisol. 92% adherence	Short duration, indirect assessment of NAFLD, specific population	Curcumin improved metabolic and liver parameters over 8 weeks.
18	(Ashraf; Rather; Mehraj, 2025)	Randomized, single-blind, standard-controlled clinical trial (vit E)	68 patients with NAFLD (50 completed the study), 60 days.	68 patients with NAFLD (50 completed the study), turmeric (1000 mg/day) vs vit E (800 mg/day), 60 days.	Curcumin improves RHC (p=0.0001), dyspepsia (p=0.0001), with no significant change for steatosis, AST/ALT	Small sample size, ultrasound evaluation, short duration, potential bias (single-blind)	Curcumin was superior to vit. E in relieving underlying symptoms in patients with NAFLD, and both reduced hepatic steatosis.
19	(Chashmniam et al., 2019)	Randomized, double-blind clinical trial	58 patients with NAFLD, 8 weeks.	250 mg/day vs placebo, 8 weeks	Reduction of metabolites, oxidative stress, inflammation.	Small sample, short duration, indirect evaluation, lack of clinical data	Reduction of oxidative stress and inflammation, improvement of energy metabolism.
20	(Mirhafez et al., 2019)	Randomized, double-blind clinical trial.	65 NAFLD patients, 8 weeks, overweight/obese	Curcumin (250 mg/day)	Increased adiponectin (p<0.001), decreased leptin (p<0.001), increased HDL, decreased LDL, AST/ALT	Small sample, short duration, low dose (250 mg/day), indirect evaluation, lack of strict control	Improved insulin sensitivity, increased adiponectin and reduced leptin
21	(Mirhafez et al., 2019)	Randomized, double-blind	55 individuals with NAFLD, 8 weeks	Curcumin 500 mg/day + piperine 5 mg/day	No significant difference in oxidative stress	Small sample, short duration, assessment method did not	It did not significantly reduce

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		clinical trial.				capture many aspects of oxidative stress	oxidative stress
22	(Saadati et al., 2019b)	Randomized clinical trial	52 patients with NAFLD, 12 weeks	Curcumin (1500 mg/day), lifestyle advice (diet and exercise)	Curcumin group, reduction in liver fibrosis (p=0.05), improvement in cholesterol, glucose and ALT (p=0.05), Other parameters with no significant difference	Small sample, short duration, effect of lifestyle changes	Improvements in liver fibrosis and some metabolic parameters.
23	(Sharifi et al., 2023)	Randomized, double-blind clinical trial.	60 participants with NAFLD, 12 weeks.	Curcumina (500 mg/dia) + piperina (5 mg/dia)	Curcumin group: significant reduction in WC, BP, TC, LDL, glycemia, AST/ALT	Small sample, short duration, indirect assessment of NAFLD	Improved BP, TC, LDL, insulin resistance, AST/ALT. No impact on liver fibrosis.
24	(He et al., 2024)	Randomized, double-blind clinical trial	80 patients, 24 weeks.	Curcumin (500 mg/day)	Reduced hepatic steatosis, metabolic and cardiometabolic improvement	Short duration, evaluation by FibroTouch (without biopsy). Although valid, does not assess inflammation/fibrosis directly	Reduced liver fat and improved metabolic parameters

Legend: BP: blood pressure; ALT: Alanine Aminotransferase ; AST: Aspartate Aminotransferase; LDL: Low-Density Lipoprotein; HDL: High-Density Lipoprotein; TC: Total Cholesterol.

The studies analyzed show that curcumin exerts hepatoprotective effects in NAFLD/NASH through multiple mechanisms of action. Most of the clinical trials reviewed (approximately 70%) observed a significant reduction in the liver enzymes ALT and AST, indicating an improvement in hepatocellular damage. Studies such as those by (Panahi et al., 2019) and (Rahmani et al., 2016) were particularly relevant in this regard, although some

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studies with lower doses (250 mg/day) or shorter duration found no statistically significant differences.

The metabolic benefits of curcumin were equally notable, with several studies reporting improvements in the lipid profile, including a reduction in LDL and triglycerides and an increase in HDL. These effects appear to be related to activation of the AMPK pathway and inhibition of fatty acid synthesis (Panahi et al., 2016). The reduction of hepatic steatosis was another consistent finding, especially in studies using phospholipid curcumin formulations or combined with piperine, which demonstrated greater efficacy.

The underlying mechanisms of action include anti-inflammatory effects (with suppression of TNF-α, IL-6 and NF-κB), antioxidant effects (reduction of markers such as 3-methyl-2-oxovaleric acid and 8-OHdG) and modulation of the intestinal microbiota (reduction of metabolites such as methylamine and trimethylamine). These findings corroborate preclinical data and reinforce curcumin's therapeutic potential.

However, the results showed significant heterogeneity, particularly in relation to liver fibrosis markers. While some studies such as (Musso et al., 2025) and (Saadati et al., 2019b) reported regression of fibrosis, others observed no significant effects. The main limitations identified included bioavailability issues, small sample size, short study duration and methodological variations in the assessment of outcomes.

Important challenges remain that need to be addressed in future research. The optimization of formulations to improve bioavailability, such as the development of nanoparticles or synthetic analogues, represents a promising line of research. Similarly, clinical trials of longer duration (greater than 24 weeks) and with more precise evaluation methods, such as liver biopsy or elastography, are needed to better characterize the effects of curcumin on disease progression.

4 CONCLUSION

In conclusion, curcumin shows a promising pharmacological profile in the management of NAFLD/NASH, with particularly relevant effects on reducing inflammation, oxidative stress and hepatic steatosis. However, the variability in results and the methodological limitations of existing studies highlight the need for further research to establish optimized therapeutic protocols and confirm its potential as a hepatoprotective agent on a large scale.

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