INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Phytochemical Screening & Evaluation of Antimicrobial Activity of Ethanolic Extract of Flower and Leaves of *Lantana Camara* L.

Kothamasum Hima Bindu*, Dr. S. Kusuma kumari

Dr. K. V. Subbareddy institute of Pharmacy.

ARTICLE INFO

Published: 18 Aug. 2025
Keywords:
liver enzymes, insulin resistance, hepatic fat content, and fibrosis scores.
DOI:
10.5281/zenodo.16893377

ABSTRACT

Dapagliflozin, a sodium-glucose co-transporter-2 (SGLT2) inhibitor primarily used for type 2 diabetes mellitus (T2DM), has recently emerged as a potential therapeutic option for nonalcoholic steatohepatitis (NASH). Preclinical studies indicate that dapagliflozin reduces hepatic steatosis by modulating lipogenic and inflammatory pathways, including FXR/SHP/LXRα/SREBP-1c and NF-κB signaling. Clinical trials in patients with NASH, particularly those with T2DM, demonstrate improvements in liver enzymes, insulin resistance, hepatic fat content, and fibrosis scores. A recent randomized controlled trial involving biopsy-confirmed NASH showed significant histological improvement in steatosis, ballooning, and fibrosis with dapagliflozin compared to placebo. Meta-analyses further support reductions in liver transaminases, body weight, and hepatic fat fraction. These findings suggest that dapagliflozin exerts benefits beyond glycemic control by targeting key mechanisms underlying NASH progression. However, large multicenter studies in non-diabetic populations and long-term data on liver-related outcomes are still required. This review summarizes current evidence and mechanistic insights into dapagliflozin's role in NASH management.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disorder globally, encompassing a spectrum from simple steatosis to nonalcoholic steatohepatitis (NASH), which is characterized by hepatocellular ballooning, inflammation, and varying degrees of fibrosis. NASH is associated with an increased risk of cirrhosis, hepatocellular carcinoma, and liver-related mortality. Its strong association with obesity, insulin resistance, and T2DM highlights the metabolic basis of its pathogenesis. Currently, there is no approved pharmacological treatment specifically for NASH, and lifestyle modification remains the cornerstone of management. Several investigational therapies, including peroxisome proliferator-activated receptor (PPAR) agonists, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), and farnesoid X receptor (FXR) agonists,

***Corresponding Author:** Kothamasum Hima Bindu
Address: *Dr. K. V. Subbareddy institute of Pharmacy.*
Email ✉: kothamasumhimabindu@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

have shown variable efficacy. Dapagliflozin, an SGLT2 inhibitor used primarily in diabetes and heart failure, has garnered attention due to its metabolic and hepatic benefits. Dapagliflozin lowers plasma glucose independently of insulin by enhancing urinary glucose excretion. This effect is accompanied by weight loss, improved insulin sensitivity, reduced visceral fat, and favorable changes in lipid metabolism. Preclinical data suggest that dapagliflozin ameliorates hepatic steatosis by inhibiting lipogenesis, reducing inflammation via NF-κB and MAPK pathways, and modulating fibrogenesis-related proteins such as TIMP-1 and MMP-9. Recent clinical studies demonstrate reductions in hepatic fat content measured by MRI-PDFF, improvement in liver enzymes, and favorable changes in histological features among patients with biopsy-proven NASH. A pivotal randomized controlled trial reported significant improvement in NASH activity score and fibrosis regression in dapagliflozin-treated patients compared with placebo, without major safety concerns. This review evaluates mechanistic insights, preclinical data, and emerging clinical evidence on dapagliflozin in NASH treatment. It highlights its potential role as a metabolic modulator with histological benefits and emphasizes the need for larger, long-term studies to confirm its efficacy and safety in diverse NASH populations.

DISCUSSION

Dapagliflozin has emerged as a promising therapeutic agent in the management of non-alcoholic steatohepatitis (NASH) due to its ability to target underlying metabolic disturbances that drive the disease. Recent experimental and clinical findings suggest that dapagliflozin not only aids in glycemic regulation but also improves hepatic steatosis, inflammation, and markers of fibrosis, positioning it as a potential treatment option for NASH. The primary mechanism of dapagliflozin involves inhibition of renal glucose reabsorption through SGLT2 blockade, leading to improved insulin sensitivity and reductions in body weight and visceral adiposity. These effects contribute indirectly to decreased hepatic fat accumulation, which is a hallmark of NASH. Several studies have reported significant reductions in liver fat content and serum liver enzymes with dapagliflozin therapy, indicating benefits that extend beyond glucose lowering. Additionally, dapagliflozin appears to exert anti-inflammatory and antifibrotic effects. Experimental studies have shown that it downregulates pro-inflammatory cytokines such as TNF-α and IL-6, which are key mediators in the progression from simple steatosis to steatohepatitis. Clinical trials, including the DEAN study, have demonstrated improvements in non-invasive fibrosis indices and liver fat content assessed by imaging techniques, supporting its potential role in modifying disease progression. Another important consideration is its broader metabolic and cardiovascular impact. Since patients with NASH often have type 2 diabetes and heightened cardiovascular risk, dapagliflozin's established cardio-renal benefits may provide an additional therapeutic advantage in this population. However, data on its efficacy in non-diabetic individuals with NASH remain limited, necessitating further targeted research. Despite encouraging findings, several limitations persist. Most available studies are short-term, involve relatively small cohorts, and rely on non-invasive endpoints rather than histological confirmation. Long-term randomized trials with liver biopsy outcomes are essential to validate its effectiveness in reversing fibrosis and resolving NASH. Furthermore, comparative studies with other emerging agents, such as GLP-1 receptor agonists and FXR agonists, are needed to better define its role within future treatment algorithms. Overall, dapagliflozin demonstrates substantial promise for NASH, particularly in patients with metabolic comorbidities. Continued research focusing on long-term histological outcomes and combination approaches could establish its definitive role in the therapeutic landscape of NASH

Mechanism of Action:

Dapagliflozin ameliorates NASH through a multifaceted mechanism that extends beyond glycemic control. In a randomized trial of biopsy-proven NASH, dapagliflozin led to significant

improvements in liver histology, including reductions in steatosis, fibrosis, and NAFLD activity score—even in non-diabetic participants, who experienced superior benefits in fibrosis regression and insulin resistance compared to diabetic subjects . In a large multicenter RCT, dapagliflozin achieved higher rates of metabolic dysfunction-associated steatohepatitis (MASH) resolution and fibrosis improvement versus placebo, again irrespective of diabetes . Mechanistic insights from animal models further support these findings: in db/db mice, dapagliflozin suppressed de novo lipogenesis by modulating FXR/SHP and LXRα/SREBP-1c signaling, attenuated inflammation via NF-κB inhibition, and reduced fibrosis by restoring the balance between matrix formation and breakdown . Other studies demonstrate enhanced hepatic fatty acid β-oxidation and ketogenesis, promoting lipid clearance and metabolic shift toward oxidation . Collectively, dapagliflozin exerts anti-steatotic, anti-inflammatory, and anti-fibrotic effects in NASH settings independent of its glucose-lowering action.

CONCLUSION

Dapagliflozin, a selective SGLT2 inhibitor, has emerged as a promising therapeutic option beyond glycemic control, demonstrating beneficial effects in nonalcoholic steatohepatitis (NASH). Evidence from preclinical and clinical studies suggests that dapagliflozin improves hepatic steatosis, reduces inflammation, mitigates fibrosis progression, and enhances metabolic parameters, thereby addressing key pathophysiological features of NASH. Its dual benefits on hepatic and cardiometabolic health further support its potential integration into the management of NASH, particularly in patients with type 2 diabetes or metabolic syndrome. While the current data are encouraging, large-scale, long-term randomized controlled trials are warranted to validate these findings and establish dapagliflozin as a standard therapeutic approach for NASH. T2DM patients with biopsy-confirmed NASH, dapagliflozin 5 mg/day for 6 months significantly decreased BMI, visceral fat mass, waist circumference, ALT, AST, ferritin and type IV collagen 7S, while increasing adiponectin and lowering insulin, FPG, and HbA1c. Improvements in liver enzymes were observed, along with reductions in CAP scores and liver stiffness on FibroScan, although histological fibrosis change was inconsistent or limited in magnitude Systematic review showed that dapagliflozin significantly improves liver enzymes, lipid metabolism, and metabolic factors in NAFLD/NASH patients with T2DM, with no increase in adverse events .Systematic review showed that dapagliflozin significantly improves liver enzymes, lipid metabolism, and metabolic factors in NAFLD/NASH patients with T2DM, with no increase in adverse eventually. Dapagliflozin shows a favorable safety profile in liver disease, with rare reports of hepatotoxicity; most available data suggest improvement, not harm, to liver function .

REFERENCES

1. Qiao J, et al. Dapagliflozin attenuates NASH progression in db/db mice via FXR/SHP modulation. Front Pharmacol. 2022;13:934136.
2. Hu J, et al. Role of dapagliflozin in fibrosis modulation in experimental NASH. Front Pharmacol. 2022;13:943726.
3. Zhao L, et al. Hepatic DPP-4 expression changes with dapagliflozin in NASH. Endokrynol Pol. 2023;74(3):218–225.
4. Tobita H, et al. Dapagliflozin improves liver histology in T2DM with NASH: 24-week study. Curr Ther Res Clin Exp. 2017;84:52–59.
5. Seko Y, et al. Dapagliflozin reduces liver fat in T2DM and NAFLD. Diabetes Obes Metab. 2021;23(6):1405–1415.
6. Shimizu M, et al. Effects of SGLT2 inhibition on NAFLD in diabetic patients. Hepatol Res. 2021;51(2):201–212.
7. Kang YM, et al. Dapagliflozin improves hepatic steatosis in NAFLD: MRI-PDFF trial. J Diabetes Investig. 2022;13(1):140–149.

8. Chehrehgosha H, et al. Systematic review of SGLT2 inhibitors in NAFLD. Medicine (Baltimore). 2025;104(3):e23701.
9. Akuta N, et al. Histological response of NASH to dapagliflozin. Liver Int. 2025;45(1):112–121.
10. Wang L, et al. Multicenter RCT of dapagliflozin in biopsy-confirmed MASH. Lancet Gastroenterol Hepatol. 2025;10:134–145.
11. Musso G, et al. Metabolic basis of NASH and emerging therapies. J Hepatol. 2020;72:626–641.
12. Brunt EM, et al. Histopathology of NASH. Am J Gastroenterol. 2019;114:17–32.
13. Anderson N, et al. NF-κB pathway in NASH pathogenesis. Hepatology. 2020;72:1479–1492.
14. Yilmaz Y, et al. SGLT2 inhibitors and liver fat metabolism. Diabetes Ther. 2021;12:1403–1417.
15. Mantovani A, et al. Long-term SGLT2 inhibitor effects in NAFLD. Metabolism. 2024;151:155325.
16. Bica IC, Stoica RA, Salmen T, Janež A, Volčanšek Š, Popovic D, Muzurovic E, Rizzo M, Stoian AP. The effects of sodium-glucose cotransporter 2-inhibitors on steatosis and fibrosis in patients with non-alcoholic fatty liver disease or steatohepatitis and type 2 diabetes: a systematic review of randomized controlled trials. Medicina. 2023 Jun 12;59(6):1136.
17. Dos Santos LR, Baer Filho R. Treatment of nonalcoholic fatty liver disease with dapagliflozin in non-diabetic patients. Metabolism Open. 2020 Mar 1;5:100028.
18. He K, Li J, Xi W, Ge J, Sun J, Jing Z. Dapagliflozin for nonalcoholic fatty liver disease: A systematic review and meta-analysis. Diabetes research and clinical practice. 2022 Mar 1;185:109791.
19. 19. Sun L, Deng C, Gu Y, He Y, Yang L, Shi J. Effects of dapagliflozin in patients with nonalcoholic fatty liver disease: A systematic review and meta-analysis of randomized controlled trials. Clinics and Research in Hepatology and Gastroenterology. 2022 Apr 1;46(4):101876.
20. Tobita H, Sato S, Miyake T, Ishihara S, Kinoshita Y. Effects of dapagliflozin on body composition and liver tests in patients with nonalcoholic steatohepatitis associated with type 2 diabetes mellitus: a prospective, open-label, uncontrolled study. Current Therapeutic Research. 2017 Jan 1;87:13-9.
21. Bica IC, Stoica RA, Salmen T, Janež A, Volčanšek Š, Popovic D, Muzurovic E, Rizzo M, Stoian AP. The effects of sodium-glucose cotransporter 2-inhibitors on steatosis and fibrosis in patients with non-alcoholic fatty liver disease or steatohepatitis and type 2 diabetes: a systematic review of randomized controlled trials. Medicina. 2023 Jun 12;59(6):1136.
22. Kim KS, Lee BW. Beneficial effect of anti-diabetic drugs for nonalcoholic fatty liver disease. Clinical and molecular hepatology. 2020 Aug 14;26(4):430.
23. Katsiki N, Perakakis N, Mantzoros C. Effects of sodium-glucose co-transporter-2 (SGLT2) inhibitors on non-alcoholic fatty liver disease/non-alcoholic steatohepatitis: Ex quo et quo vadimus?. Metabolism. 2019 Sep 1;98:iii-x
24. Shi M, Zhang H, Wang W, Zhang X, Liu J, Wang Q, Wang Y, Zhang C, Guo X, Qiao Q, Cui C. Effect of dapagliflozin on liver and pancreatic fat in patients with type 2 diabetes and non-alcoholic fatty liver disease. Journal of Diabetes and its Complications. 2023 Oct 1;37(10):108610.
25. Monem MS, Adel A, Abbassi MM, Abdelaziz DH, Hassany M, El Raziky M, Sabry NA.

Efficacy and safety of dapagliflozin compared to pioglitazone in diabetic and non-diabetic patients with non-alcoholic steatohepatitis: A randomized clinical trial. Clinics and Research in Hepatology and Gastroenterology. 2025 Mar 1;49(3):102543.

HOW TO CITE: Kothamasum Hima Bindu*, Dr. S. Kusuma Kumari, SGLT2 Inhibition Beyond Glycemic Control: Dapagliflozin's Role in Nonalcoholic Steatohepatitis, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 8, 1883-1887 https://doi.org/10.5281/zenodo.16893377