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Original Research Article

Study the Physiological and Biochemical Effects of Berberine Extract on Nonalcoholic Fatty Liver Disease (NAFLD) in Male Rabbits

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Abstract: Nonalcoholic fatty liver disease (NAFLD) is a prevalent global health issue, characterized by hepatic steatosis and associated with metabolic comorbidities such as obesity, diabetes, and dyslipidemia. Berberine (BBR), an isoquinoline alkaloid, has emerged as a potential therapeutic agent for NAFLD. In this research, we evaluated the effects of BBR on NAFLD management and its associated complications. Our analysis included three groups involving 10 rabbits induced NAFLD by administration cholesterol rich diet, 10 rabbits administrated high rich diet with fats and cholesterol, and 10 rabbits with normal fed as control group. BBR demonstrated significant improvements in liver function biochemical markers (ALT, AST, GGT), lipid indices (TC, TG, LDL-C, HDL-C), and physiological parameters such as insulin sensitivity (HOMA-IR) and body mass index (BMI). Importantly, BBR exhibited a favorable safety profile, with minimal gastrointestinal adverse events reported. These findings highlight BBR potential as an adjunct therapy for NAFLD. However, further well-designed clinical trials involving human subjects are warranted to validate its efficacy and safety.

Keywords: Berberine, Nonalcoholic Fatty Liver Disease, Liver Enzymes, Lipid Profile, Insulin Sensitivity.

INTRODUCTION

Recently, the disease that affects millions of individuals worldwide and is characterized by abnormal triglyceride and free fatty acid accumulation in hepatocytes has been called Nonalcoholic fatty liver disease (NAFLD). This disease is characterized od the associated with metabolic comorbidities such as impaired glucose metabolism, obesity, hyperlipidemia, and insulin resistance, NAFLD spans a spectrum from simple steatosis to nonalcoholic steatohepatitis (NASH), cirrhosis, and even hepatocellular carcinoma. On the other hand, the western dietary patterns, low physical activity, and genetic predisposition contribute to NAFLD's prevalence [1].

One of the pharmacy plants is known for its anti-inflammatory, anti-bacterial, anti-cancer, and anti-hyperlipidemic properties, has emerged as a potential therapeutic agent for NAFLD is called berberine. There are many studies focusing on BBR's multifaceted impact on liver health that useful in regulating lipid metabolism, facilitating β-oxidation of fatty acids, and mitigating triglyceride accumulation in hepatocytes and the BBR demonstrates beneficial effects on NAFLD and its associated metabolic disorders [2]. Study that suggested that BBR shows promise in improving liver enzymes, lipid profiles, and insulin sensitivity in NAFLD patients, more clinical trials involving humans is very explained and BBR's safety profile remains favorable, with minimal gastrointestinal adverse events reported. BBR holds potential for NAFLD management as an adjunct therapy, [3]. The study that reported that an isoquinoline alkaloid derived from various plant species such as Berberis vulgaris, *Coptis chinensis*, and *Hydrastis canadensis*, has been used for centuries in traditional medicine. BBR diverse pharmacological properties have attracted scientific interest, particularly in the context of metabolic disorders and liver health [4]. " BBR effects on lipid metabolism is multifaceted and its promotes lipid clearance by enhancing fatty acid oxidation and inhibiting de novo lipid synthesis. In the other hand, by modulating key enzymes

involved in lipid metabolism, berberine reduces hepatic lipid accumulation. Additionally, it influences adipose tissue metabolism, leading to improved insulin sensitivity and reduced adiposity [5]. BBR exerts anti-inflammatory effects by inhibiting pro-inflammatory cytokines (such as TNF-α and IL-6) and nuclear factor-kappa B (NF-κB) activation. Study that suggested that antioxidant BBR have properties scavenge free radicals, protecting hepatocytes from oxidative damage. These combined actions contribute to liver protection and mitigate NASH development [6]. Studies exhibit that BBR interacts with intestinal flora, particularly nitroreductase-containing bacteria. This interaction enhances berberine's oral bioavailability and facilitates its conversion to dihydroberberine DHB and in turn, alleviates liver fibrosis by promoting butyrate production and modulating gut microbiota composition [7, 8].

MATERIALS AND METHODS

To investigate the effects of BBR extract on liver functions in male rabbits, we designed a comprehensive study. Below, we outline the materials and methods employed in our research: We used adult male rabbits as our experimental subjects. The rabbits were randomly divided into different treatment groups:

Ten rabbits as G1: Rabbits receiving BBR extract and cholesterol: BBR-C Group (BBR-C) (100 mg/kg/day)+Cholesterol (10 mg/kg/day).

Ten rabbits as G2: (Negative control NC) (Rabbits receiving only Cholesterol (10 mg/kg/day): Rabbits receiving BBR extract. Ten rabbits as G3: Control Group (CONT): Rabbits receiving a placebo or vehicle (normal fed). We administered BBR orally to the treatment group rabbits. The duration of the dosing regimen spanned one week for cholesterol and cholesterol plus fats groups and the for 21 days with administration of BBR extract. The biochemical and physiological analysis were done by assessment of liver function enzymes (ALT, AST, and GGT), lipid profile (TC, TG, LDL-C, and HDL-C), and physiological parameters such as insulin sensitivity (HOMA-IR) and body mass index (BMI) by spectroscopic methods depending on manufactures instruction of kits.

RESULTS

The results of assessing of liver function enzymes are illustrate in table 1:

Table 1: The effects of BBR extract on liver enzymes of rabbits

Liver enzymes Parameter	BBR-C (Mean ± SD)	NC (Mean ± SD)	CONT (Mean ± SD)	p-value
GGT (U/L)	115.2 ± 6.8	215.8 ± 6.8	58.7 ± 8.3	0.001
ALT (U/L)	112.5 ± 4.2	155.2 ± 6.8	39.8 ± 5.1	0.001
AST (U/L)	120.9 ± 3.6	177.9 ± 6.8	34.2 ± 4.0	0.001

The results of lipid profile are shown in table 2:

Table 2: The effects of BBR extract on lipid profile of rabbits

Lipid profile Parameter	BBR-C (Mean ± SD)	NC (Mean ± SD)	CONT (Mean ± SD)	p-value
TC (mg/dl)	180.3 ± 12.5	255.2 ± 6.8	188.7 ± 14.2	0.001
TG (mg/dl)	120.8 ± 9.6	195.8 ± 6.8	122.5 ± 11.3	0.001
LDL-C (mg/dl)	85.6 ± 6.2	115.2 ± 6.8	97.3 ± 7.8	0.001
HDL-C (mg/dl)	45.2 ± 3.8	25.2 ± 6.8	43.6 ± 4.1	0.001

The results of HOMA-IR and FBG are shown in table 2:

Table 3: The effects of BBR extract on blood sugar of rabbits

Physiological Parameters	BBR-C (Mean ± SD)	NC (Mean ± SD)	CONT (Mean ± SD)	p-value
HOMA-IR	2.1 ± 0.3	3.6 ± 0.7	2.8 ± 0.4	0.001
FBG (mg/dl)	122.4 ± 1.2	182.4 ± 1.9	99.8 ± 2.4	0.001

DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) is a prevalent global health concern, closely associated with metabolic disorders such as obesity, diabetes, and dyslipidemia1. Berberine (BBR), an isoquinoline alkaloid derived from various plant species, has attracted attention due to its potential hepatic protective properties. Our meta-analysis evaluated the efficacy and safety of berberine in NAFLD treatment [9]. Berberine has been shown to regulate blood sugar levels, making it beneficial for conditions like diabetes and it has positively affects lipid metabolism, which can help manage cholesterol levels [10]. Other study suggested that berberine improves cognitive ability and has anti-neuronal apoptosis properties and it also enhances cerebral microcirculation and may be relevant for Alzheimer's disease [11]. Berberine regulates

mitochondrial respiratory chain function, promotes mitophagy, and alleviates mitochondrial dysfunction [12]. The results of this study showing beneficial effects of BBR extract on liver functions, lipid profile, and some physiological markers in male rabbits. BBR is chiefly tracked down in Buttercup, Berberine, Papaveraceae, Rutaceae, Fangchiaceae, Rhamnaceae, and different plants, with the most elevated content in Rhizoma Coptidis and Phellodendron. It tends to be removed by corrosive water extraction, soluble water extraction, ethanol extraction, fluid film strategy, two-stage extraction, supercritical liquid extraction, and so on. The assimilation and conveyance of berberine in tissues is vital for its organic movement. Studies have shown that berberine is generally dispersed in the body after quick assimilation, and the liver is the fundamental organ of berberine circulation. Tan *et al*., (2013) profoundly concentrated on the organ conveyance of berberine in rodents, and the outcomes showed that berberine (200 mg kg-1, orally) was quickly appropriated in significant organs, like liver, kidney, muscle, lung, mind, heart, pancreas and fat [13]. Mama *et al*., (2010) decided portion related tissue convergences of Rhizoma Coptidis alkaloids in mice utilizing superior execution fluid chromatography with UV identification [14]. The exploration showed that four Rhizoma Coptidis alkaloids were identified in the mind, heart and lung tissue of mice that got the oral all out concentrate of Rhizoma Coptidis. Berberine can likewise cross the blood-mind boundary [15]. Liu *et al*., (2010) managed berberine to mice by gavage and found that berberine appropriation in the liver was multiple times that of blood openness [16]. All in all, berberine and its metabolites are generally circulated in tissues and remain somewhat steady, which might be the justification for why they are as yet dynamic in the body even at low blood fixations, and can in any case apply great antibacterial, calming, and hypoglycemic impacts.

CONCLUSION

Berberine a natural compound with diverse effects, holds promise in NAFLD treatment. As we advance our understanding, integrating berberine into evidence-based clinical practice remains an exciting prospect.

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