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FORMULATION AND EVALUATION OF A MULTI NUTRITIONAL HERBAL DRUG FOR NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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1. ABSTRACT

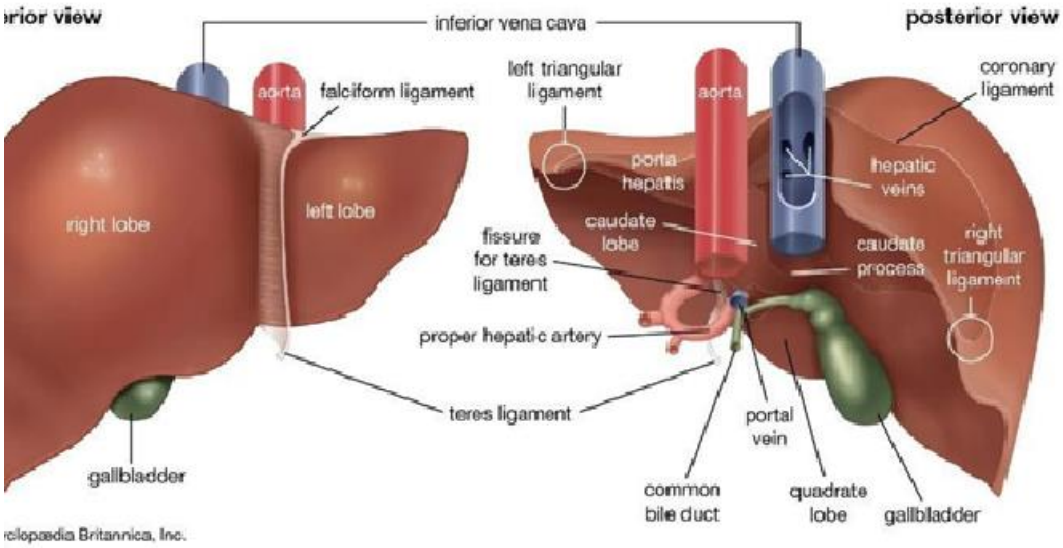
In this project, we focused on the formulation and evaluation of a nutraceutical capsule for the management of Non-Alcoholic Fatty Liver Disease (NAFLD), also known as Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). NAFLD is a rapidly increasing liver disorder associated with obesity, insulin resistance, diabetes, and unhealthy lifestyle habits. Due to the lack of a specific approved pharmacological treatment for NAFLD, we aimed to develop a safer and effective nutraceutical formulation using natural bioactive compounds. For this study, we selected Berberine and Curcumin as active pharmaceutical ingredients because of their hepatoprotective, antioxidant, anti-inflammatory, and lipid-lowering properties. Berberine is known to improve insulin sensitivity and reduce hepatic lipid accumulation, while curcumin helps in reducing oxidative stress and inflammation in liver tissues. The combination of these two compounds was expected to provide synergistic therapeutic benefits in NAFLD management. The nutraceutical capsules were formulated using suitable excipients and evaluated for various preformulation and postformulation parameters including organoleptic properties, flow properties, weight variation, disintegration time, and drug content. UV-visible spectrophotometry was performed for analytical estimation of berberine and curcumin using standard calibration curves at their respective wavelengths. From the evaluation studies, we observed that the formulated capsules exhibited satisfactory pharmaceutical characteristics and may help in improving liver health by reducing oxidative

stress, inflammation, and lipid accumulation. Therefore, the developed nutraceutical capsule formulation may serve as a promising supportive therapeutic approach for the management of NAFLD.

KEYWORDS: Berberine, Curcumin, Hepatoprotective Activity, Liver Disorders, NAFLD, Nutraceutical Capsule, UV Spectrophotometry.

1. INTRODUCTION

1.1. Anatomy & Physiology of Liver



2. 1. Anatomy & Physiology of Liver.

1.1.1. Liver

The liver is the largest gland in the human body and is situated in the right upper quadrant of the abdomen, just below the diaphragm. It extends slightly towards the left side and is protected by the ribcage. In adults, the liver weighs approximately 1.4 – 1.8 kg, contributing around 2 – 3% of total body weight. It is covered by a fibrous connective tissue layer known as Glisson's capsule, which provides structural support and protection.[1]

1.1.2. Lobes and Ligaments

Anatomically, the liver is divided into right and left lobes, with additional caudate and quadrate lobes. These lobes are separated by structures such as the falciform ligament. The liver is held in position by peritoneal ligaments including the falciform, coronary, and triangular ligaments, which anchor it to the diaphragm and anterior abdominal wall.[3]

1.1.3. Blood Supply and Circulation

The liver has a unique dual blood supply that is essential for its metabolic functions. The portal vein supplies about 70–75% of blood, which is rich in nutrients absorbed from the gastrointestinal tract, while the hepatic artery provides 25–30% oxygenated blood. Blood flows through specialized capillaries called sinusoids, allowing efficient exchange of substances, and then drains into the central vein and ultimately into the inferior vena cava.[2]

1.1.4. Microscopic Structure

The structural and functional unit of the liver is the hepatic lobule. It consists of hepatocytes arranged in plates, a central vein, and sinusoids. Each lobule also contains a portal triad made up of branches of the hepatic artery, portal vein, and bile duct. Various cell types are present, including hepatocytes (main metabolic cells), Kupffer cells (immune cells), stellate cells (involved in storage and fibrosis), endothelial cells, and cholangiocytes lining the bile ducts.

1.1.5. Metabolic Functions

The liver plays a central role in metabolism. It regulates carbohydrate metabolism by maintaining blood glucose levels through glycogenesis, glycogenolysis, and gluconeogenesis. It is also involved in protein metabolism, including deamination of amino acids, urea formation, and synthesis of plasma proteins such as albumin and clotting factors. Additionally, the liver is essential for lipid metabolism, including cholesterol synthesis, lipoprotein formation, and fatty acid oxidation.

1.1.6. Bile Production and Digestion

The liver produces bile, which is crucial for digestion. Bile helps in the emulsification of fats, making them easier to digest and absorb. It also facilitates the absorption of fat-soluble vitamins (A, D, E, and K) and plays a role in the excretion of bilirubin and other waste products.

1.1.7. Detoxification Function

One of the most important functions of the liver is detoxification. It metabolizes drugs, toxins, and harmful substances, converting them into less toxic, water-soluble forms that can be easily excreted through urine or bile. This function is essential for protecting the body from harmful chemicals and maintaining internal balance.

1.1.8. Storage Function

The liver acts as a storage organ for essential nutrients. It stores glycogen as an energy reserve

and also stores vitamins such as A, D, and B12, along with minerals like iron and copper. These stored substances are released when required by the body.

1.1.9. Immune and Hormonal Functions

The liver contributes to immune defense through Kupffer cells, which remove bacteria and foreign particles from the blood. It also plays a role in hormone regulation by metabolizing hormones such as insulin and steroid hormones, thereby maintaining hormonal balance in the body.[4][5][6]

1.2. Overview of NAFLD: Non-alcoholic fatty liver disease (NAFLD) is a chronic and progressive metabolic liver disorder characterized by excessive accumulation of triglycerides in hepatocytes (liver cells) in individuals who consume little or no alcohol. It is one of the most prevalent liver diseases worldwide, affecting nearly 25% of the global adult population. NAFLD is strongly associated with metabolic disorders such as obesity, type 2 diabetes mellitus, dyslipidaemia, and hypertension, and is often considered the hepatic manifestation of metabolic syndrome.

NAFLD encompasses a broad spectrum of liver conditions ranging from simple steatosis (fat accumulation without inflammation) to non-alcoholic steatohepatitis (NASH), which involves inflammation, hepatocellular injury, and fibrosis. While simple steatosis is relatively benign, NASH can progress to advanced stages such as liver fibrosis, cirrhosis, and even hepatocellular carcinoma (HCC). Disease progression is influenced by multiple factors, and nearly one-third of patients may advance to severe forms over time.

The pathogenesis of NAFLD is complex and multifactorial, commonly explained by the "multiple-hit hypothesis." The initial "hit" involves insulin resistance, leading to increased free fatty acid (FFA) influx into the liver, enhanced de novo lipogenesis, and reduced fatty acid oxidation, resulting in lipid accumulation. Subsequent "hits" include oxidative stress, mitochondrial dysfunction, inflammation, and gut microbiota imbalance, which collectively promote liver injury and disease progression. Reactive oxygen species (ROS) play a central role by inducing cellular damage, inflammation, and fibrosis.

At the molecular level, dysregulation of lipid metabolism is a key feature, where triglycerides accumulate due to excess fatty acid supply from adipose tissue, dietary sources, and increased hepatic synthesis. Insulin resistance further exacerbates this process by increasing lipolysis and

impairing glucose metabolism. In addition, pro- inflammatory cytokines such as TNF-α and interleukins contribute to hepatic inflammation, while mitochondrial dysfunction and endoplasmic reticulum stress intensify oxidative damage.

NAFLD is often asymptomatic in its early stages and is frequently diagnosed incidentally through imaging techniques or abnormal liver function tests. Due to the lack of specific pharmacological treatments, management primarily focuses on lifestyle modifications such as weight loss, dietary changes, and regular physical activity. Early intervention is crucial, as advanced stages like cirrhosis are often irreversible. Overall, NAFLD represents a significant global health challenge due to its high prevalence, silent progression, and strong association with metabolic diseases.[7][8][9][10]

1.2.1. Types of NAFLD

Non-Alcoholic Fatty Liver Disease (NAFLD), now more commonly known as Metabolic Dysfunction– Associated Steatotic Liver Disease (MASLD), is a condition in which excess fat builds up in the liver in people who consume little or no alcohol. The disease can range from a mild fatty liver to severe liver damage over time.

1.2.1.1. Simple Steatosis (NAFL)

Also known as Non-Alcoholic Fatty Liver (NAFL), this is the earliest and mildest form of the disease.

In this stage, fat starts accumulating inside the liver cells, but there is little or no inflammation or damage to the liver tissue. Most people do not experience symptoms, and the condition is often discovered accidentally during routine tests or scans. Although considered relatively harmless initially, it can progress further if risk factors such as obesity, diabetes, poor diet, or lack of physical activity continue.

1.2.1.2. Non-Alcoholic Steatohepatitis (NASH/MASH)

This stage is now called Metabolic Dysfunction–Associated Steatohepatitis (MASH)

Here, fat accumulation in the liver is accompanied by inflammation and injury to liver cells. The liver cells may become swollen and damaged, a process known as hepatocyte ballooning. Compared to simple steatosis, this form is more serious because ongoing inflammation can gradually lead to scarring of the liver.

If left untreated, MASH may progress to fibrosis, cirrhosis, or even liver cancer.

1.2.1.3 Fibrotic NAFLD

When liver inflammation continues for a long period, scar tissue begins to form in the liver. This stage is called fibrotic NAFLD.

Fibrosis is graded into stages depending on the severity of scarring:

- F0 – No fibrosis
- F1 – Mild fibrosis
- F2 – Moderate fibrosis
- F3 – Severe or bridging fibrosis
- F4 – Cirrhosis

Advanced fibrosis is clinically important because it increases the risk of serious liver complications and reduces liver function over time.

1.2.1.4. Cirrhotic NAFLD

This is the most advanced stage of the disease.

In cirrhosis, extensive scarring permanently damages the structure and function of the liver. The liver becomes stiff and unable to perform its normal metabolic and detoxification functions efficiently.

Patients with cirrhotic NAFLD may develop complications such as:

- Portal hypertension
- Liver failure
- Fluid accumulation in the abdomen
- Bleeding complications
- Hepatocellular carcinoma (liver cancer)

Today, MASLD/MASH is considered one of the leading causes of chronic liver disease and cirrhosis worldwide.[12][13][14]

1.3. Roles of Neutraceuticals in NAFLD management

Non-alcoholic fatty liver disease (NAFLD) is a chronic metabolic liver disorder characterized by the abnormal accumulation of fat, primarily triglycerides, within hepatocytes in individuals who consume little or no alcohol. It is strongly associated with conditions such as obesity, insulin resistance, type 2 diabetes mellitus, and dyslipidemia, making it a key component of metabolic syndrome. Over the past few decades, NAFLD has emerged as one of the leading

causes of liver-related morbidity worldwide. The disease ranges from simple steatosis (fat accumulation without inflammation) to more severe forms such as non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma. Due to its silent progression and lack of specific pharmacological treatments, there is increasing interest in alternative therapeutic approaches, particularly nutraceuticals. Nutraceuticals are naturally derived bioactive compounds obtained from foods, plants, or herbal sources that provide health benefits beyond basic nutrition. In the context of NAFLD, these compounds are especially valuable because they target multiple pathological mechanisms simultaneously. The development and progression of NAFLD involve complex processes such as oxidative stress, chronic inflammation, lipid metabolism imbalance, mitochondrial dysfunction, and insulin resistance. Nutraceuticals can modulate these pathways through antioxidant, anti-inflammatory, lipid-lowering, and insulin-sensitizing actions, thereby offering a holistic and supportive strategy for disease management. One of the most critical factors in NAFLD progression is oxidative stress, which arises due to excessive production of reactive oxygen species (ROS) in the liver. These reactive molecules damage cellular structures, including lipids, proteins, and DNA, ultimately leading to hepatocellular injury. Nutraceuticals such as Spirulina maxima play a protective role by neutralizing free radicals and reducing lipid peroxidation. In addition to its antioxidant effects, Spirulina also helps regulate lipid metabolism by decreasing triglyceride accumulation and enhancing fatty acid oxidation. This dual action not only protects liver cells but also reduces the burden of fat deposition in the liver. Another widely studied nutraceutical is olive oil, particularly extra virgin olive oil, which is rich in monounsaturated fatty acids and polyphenolic compounds. These components contribute to improved lipid profiles by lowering harmful low-density lipoprotein (LDL) levels and increasing beneficial high-density lipoprotein (HDL) levels. Olive oil also enhances insulin sensitivity and reduces hepatic fat accumulation. Its antioxidant and anti-inflammatory properties further help in protecting liver tissues from damage. The Mediterranean diet, which includes olive oil as a primary fat source, has been consistently associated with reduced liver fat content and improved metabolic health in individuals with NAFLD.

Berberine, a bioactive alkaloid obtained from plants such as Berberis species, has gained attention due to its strong effects on glucose and lipid metabolism. It activates the AMP-activated protein kinase (AMPK) pathway, which plays a crucial role in regulating energy balance within cells. Activation of this pathway leads to decreased lipid synthesis and increased fatty acid oxidation in the liver. Additionally, berberine improves insulin sensitivity and helps

reduce inflammation by inhibiting pro-inflammatory cytokines. It also positively influences gut microbiota, which is increasingly recognized as an important factor in NAFLD pathogenesis. Through these combined actions, berberine effectively reduces liver fat accumulation and improves overall liver function.[15][16][17]

1.4. Berberine as a Therapeutic Agent in NAFLD

Berberine, a natural isoquinoline alkaloid derived from medicinal plants such as Berberis species, has gained significant attention as a potential therapeutic agent in the management of non-alcoholic fatty liver disease (NAFLD). NAFLD is a complex metabolic disorder characterized by excessive fat accumulation in the liver and is closely associated with insulin resistance, dyslipidemia, and chronic inflammation. Due to the absence of specific approved pharmacological treatments, natural compounds like berberine are increasingly being explored for their multi-targeted therapeutic effects. Berberine demonstrates beneficial effects in NAFLD primarily through its ability to improve metabolic dysfunction. One of its key mechanisms involves enhancing insulin sensitivity, which plays a central role in the development of NAFLD. By reducing insulin resistance, berberine helps regulate glucose metabolism and decreases the excessive influx of free fatty acids into the liver. This ultimately leads to a reduction in hepatic fat accumulation and improvement in overall metabolic balance. In addition to its effects on glucose metabolism, berberine has been shown to improve lipid profiles in individuals with NAFLD. It reduces levels of triglycerides and harmful lipoproteins while promoting better lipid utilization in the liver. These actions contribute to decreased fat deposition in hepatocytes and support the restoration of normal liver function. Clinical observations have also reported improvements in liver enzyme levels, such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), indicating reduced liver injury following berberine treatment. Another important aspect of berberine's therapeutic role is its anti-inflammatory activity. Chronic low-grade inflammation is a major driver of NAFLD progression from simple steatosis to more severe conditions like non-alcoholic steatohepatitis (NASH). Berberine helps reduce systemic inflammation, as evidenced by decreased levels of inflammatory markers such as C-reactive protein (CRP). By limiting inflammatory responses, it protects liver cells from further damage and slows disease progression. Furthermore, berberine may influence liver health by modulating various biochemical and clinical parameters. Comprehensive evaluation of its therapeutic effects includes monitoring biomarkers such as fasting insulin, blood glucose levels, liver enzymes, and lipid profiles. Advanced diagnostic tools like imaging techniques and liver stiffness measurements can also

be used to assess improvements in hepatic fat content and fibrosis. These evaluations highlight the broad impact of berberine on both metabolic and structural aspects of liver disease. Despite its promising benefits, certain considerations remain important in the clinical application of berberine. Factors such as dosage, duration of treatment, and route of administration can influence its effectiveness and bioavailability. Additionally, well-designed clinical studies with standardized methodologies are necessary to establish its long- term safety and therapeutic efficacy. Improved research approaches, including better patient characterization and consistent outcome measures, are essential for validating its role in NAFLD management. In conclusion, berberine represents a promising natural therapeutic agent for NAFLD due to its ability to target multiple underlying mechanisms, including insulin resistance, lipid metabolism imbalance, and inflammation. Its multifaceted actions contribute to improved liver function and metabolic health. When combined with lifestyle modifications such as diet and exercise, berberine has the potential to play a significant role in the effective management of NAFLD. However, further clinical research is required to fully establish its therapeutic potential and optimize its use in clinical practice.[18][19][20]

1.5. Curcumin as a hepatoprotective nutraceutical in NAFLD

Non-alcoholic fatty liver disease (NAFLD) is a widespread metabolic liver disorder characterized by excessive fat accumulation in hepatocytes in the absence of significant alcohol intake. It is strongly associated with obesity, insulin resistance, and type 2 diabetes mellitus, and can progress from simple steatosis to more severe stages such as non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis. The pathogenesis of NAFLD is complex and involves multiple factors, including oxidative stress, mitochondrial dysfunction, and chronic inflammation. Since no definitive pharmacological treatment is currently available, increasing attention has been directed toward natural compounds like curcumin for their hepatoprotective potential. Curcumin, the principal bioactive component of turmeric (Curcuma longa), is widely recognized for its antioxidant and anti-inflammatory properties. It plays a significant role in protecting liver cells from damage by targeting key mechanisms involved in NAFLD progression. One of the major contributors to liver injury in NAFLD is oxidative stress, which results from an imbalance between reactive oxygen species (ROS) production and antioxidant defenses. Curcumin helps neutralize these reactive molecules, thereby reducing cellular damage and maintaining hepatic integrity.

In addition to its antioxidant activity, curcumin exhibits strong anti-inflammatory effects,

which are crucial in preventing the progression of NAFLD. Chronic inflammation in the liver is mediated by pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNF-α) and signaling pathways like nuclear factor-kappa B (NF- κB). Curcumin has been shown to suppress the activation of NF-κB and reduce the levels of inflammatory mediators, thereby limiting liver inflammation and injury. This action helps prevent the transition from simple steatosis to more severe inflammatory conditions such as NASH. Clinical studies have also demonstrated that curcumin supplementation can improve various biochemical and hepatic parameters in individuals with NAFLD. It has been associated with reductions in liver enzyme levels, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which are markers of liver damage. Additionally, curcumin may help reduce hepatic fat accumulation and fibrosis, contributing to improved liver structure and function. However, some findings suggest that when combined with lifestyle modifications such as diet and exercise, the additional benefits of curcumin may not always be significantly greater than lifestyle changes alone. Another important aspect of curcumin's hepatoprotective role is its influence on metabolic factors associated with NAFLD. It has been shown to improve insulin sensitivity and regulate lipid metabolism, thereby reducing fat deposition in the liver. By addressing both metabolic and inflammatory components of the disease, curcumin offers a comprehensive approach to NAFLD management. Despite its promising therapeutic potential, certain limitations exist in the clinical use of curcumin, including its relatively low bioavailability. Advances in formulation, such as enhanced bioavailable preparations, may help overcome these challenges and improve its clinical efficacy.

In conclusion, curcumin represents a valuable hepatoprotective nutraceutical in the management of NAFLD due to its antioxidant, anti-inflammatory, and metabolic regulatory properties. While it shows considerable promise as a supportive therapy, especially when combined with lifestyle interventions, further research is required to establish optimal dosing strategies and long-term clinical benefits.[18][19][20]

1.6. Rationale for combination therapy (Berberine +Curcumin)

Non-alcoholic fatty liver disease (NAFLD) is a complex and multifactorial disorder involving interconnected mechanisms such as insulin resistance, lipid accumulation, oxidative stress, and chronic inflammation. Because of this multi-hit pathogenesis, targeting a single pathway often provides limited therapeutic benefit. This has led to growing interest in combination therapy, where two or more agents with complementary mechanisms of action are used together to

achieve a more effective and comprehensive treatment outcome.

Combination therapy is particularly valuable in NAFLD because different therapeutic agents can act on distinct yet overlapping biological pathways. For instance, one compound may primarily improve insulin sensitivity and regulate glucose metabolism, while another may exert strong antioxidant and anti-inflammatory effects. When used together, these agents can synergistically reduce hepatic fat accumulation, decrease oxidative damage, and suppress inflammatory responses more effectively than monotherapy. This multi-targeted approach aligns well with the underlying pathophysiology of NAFLD, where multiple factors contribute simultaneously to disease progression. Another important rationale for combination therapy is the potential to enhance therapeutic efficacy while minimizing side effects. Lower doses of individual agents can often be used in combination, reducing the risk of toxicity associated with higher doses of a single drug. Additionally, combination approaches may help overcome limitations such as poor bioavailability or partial effectiveness of certain compounds when used alone. Natural compounds, particularly nutraceuticals, are increasingly being explored in combination strategies due to their safety profile and diverse biological activities. For example, combining agents with lipid-lowering, antioxidant, and anti-inflammatory properties can provide a more balanced and holistic treatment approach. This is especially relevant in NAFLD, where long-term management is required and safety is a key concern. In conclusion, combination therapy offers a rational and promising strategy for NAFLD management by addressing multiple disease mechanisms simultaneously. It enhances therapeutic outcomes, reduces limitations of single- agent therapy, and provides a more comprehensive approach to controlling disease progression.[21][22][23]

1.7. NAFLD Multinutrient Capsule Containing Berberine and Curcumin

Introduction

Non-Alcoholic Fatty Liver Disease (NAFLD), now more commonly called Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD), is a condition in which excess fat builds up in the liver in people who consume little or no alcohol. Over time, this fat accumulation can damage the liver and may lead to inflammation, fibrosis, or even cirrhosis.

NAFLD develops due to several interconnected factors such as

- insulin resistance,
- abnormal lipid metabolism,

- oxidative stress,
- chronic inflammation,
- liver cell injury.

A multinutrient capsule containing Berberine and Curcumin has shown promising benefits in the management of NAFLD because both compounds act on multiple disease-causing pathways simultaneously. They help reduce fat accumulation in the liver, decrease inflammation, protect liver cells from damage, and improve overall liver function.

1.7.1. Mechanism of Action

1.7.1.1. Mechanism of Action of Berberine

Berberine is a natural plant compound obtained from plants of the Berberis species. It is widely known for its beneficial effects on metabolism, blood sugar regulation, and liver health.

1.7.1.2. Activation of AMPK Pathway

Berberine activates AMP-activated protein kinase (AMPK), often called the body's "metabolic master switch." Activation of AMPK helps:

- reduce fat production in the liver,
- increase breakdown of fatty acids,
- decrease triglyceride formation
- improve glucose utilization.

As a result, less fat accumulates in liver cells, helping improve fatty liver changes.

1.7.1.3. Improvement of Insulin Sensitivity

Berberine helps the body respond better to insulin by improving glucose uptake and insulin receptor activity. Since insulin resistance is one of the major causes of NAFLD, improving insulin sensitivity helps slow disease progression.

1.7.1.4. Reduction of Fat Formation

Berberine suppresses enzymes and transcription factors responsible for fat synthesis in the liver, including:

- SREBP-1c,
- ACC,
- FAS

This reduces new fat formation and prevents excessive lipid deposition in hepatocytes.

1.7.1.5. Anti-Inflammatory Effect

Berberine decreases liver inflammation by inhibiting inflammatory mediators such as:

- NF-κB,
- TNF-α,
- IL-6

This helps prevent progression from simple fatty liver to inflammatory liver disease (MASH).

1.7.1.6. Mechanism of Action of Curcumin

Curcumin is the main active compound present in turmeric (Curcuma longa). It is well known for its strong antioxidant and anti-inflammatory properties.

1.7.1.7. Anti-Inflammatory Action

Curcumin helps reduce liver inflammation by blocking inflammatory pathways and mediators such as:

- NF-κB,
- COX-2,
- TNF-α,
- IL-1β.

This prevents worsening of fatty liver disease and reduces liver cell injury.

1.7.1.8. Antioxidant Effect

Curcumin boosts the body's natural antioxidant defense system by increasing enzymes like:

- Superoxide Dismutase (SOD),
- Catalase,
- Glutathione Peroxidase

It also neutralizes harmful free radicals, thereby protecting liver cells from oxidative stress.

1.7.1.9. Regulation of Lipid Metabolism

Curcumin helps maintain healthy lipid metabolism by:

- Decreasing fat synthesis,
- Increasing fatty acid breakdown,
- Reducing triglyceride and cholesterol accumulation in the liver. This contributes to reduction of hepatic steatosis.

1.71.10 Prevention of Fibrosis

Curcumin inhibits activation of hepatic stellate cells, which are responsible for liver scarring. Therefore, it may help prevent fibrosis and cirrhosis in chronic NAFLD.

1.71.11 Improvement of Gut–Liver Axis

Curcumin improves intestinal barrier function and reduces toxin-mediated inflammation originating from the gut, thereby providing additional liver protection.

1.71.12 Combined Effect of Berberine and Curcumin

When used together in a multinutrient capsule, Berberine and Curcumin work synergistically to:

Reduce fat accumulation in the liver,

- Improve insulin sensitivity,
- Decrease inflammation,
- Reduce oxidative stress,
- Protect liver cells,
- And prevent fibrosis progression.

Due to these multitarget actions, the combination may help improve overall liver health and slow the progression of NAFLD/MASLD.[24][25][26]

2. LITERATURE REVIEW

2.1. Prasad, S., and B. B. Aggarwal"Curcumin: Biological and Therapeutic Actions and Safety." Phytotherapy Research, vol. 30, no. 8, 2018, pp. 1098–1119:

Curcumin, the principal bioactive constituent of turmeric (Curcuma longa), has gained significant attention because of its diverse pharmacological and therapeutic properties. In the review article by Sanjiv Prasad and Bharat B. Aggarwal titled "Curcumin: Biological and Therapeutic Actions and Safety", the authors comprehensively discussed the biological activities, molecular targets, therapeutic potential, and safety profile of curcumin. The review highlighted that curcumin possesses potent anti-inflammatory, antioxidant, antimicrobial, anticancer, and hepatoprotective activities. The compound exerts its effects by modulating several molecular targets such as transcription factors, cytokines, enzymes, growth factors, and protein kinases. Curcumin was reported to inhibit inflammatory mediators including Nuclear Factor-kappa B (NF-κB), Cyclooxygenase-2 (COX-2), Tumor Necrosis Factor-alpha (TNF-α), and various interleukins, thereby reducing inflammation and oxidative stress.

2.2. Thoorens G, Krier F, Leclercq B, et al. "Microcrystalline Cellulose, a Direct Compression Binder in a Quality by Design Environment." International Journal of Pharmaceutics, 2014

Thoorens et al. discussed the importance of microcrystalline cellulose (MCC) as one of the most widely used pharmaceutical excipients in direct compression technology. The study focused on the functional properties of MCC in a Quality by Design (QbD) environment and highlighted its role in improving tablet formulation and manufacturing performance.

2.3. Kotta, S., et al. "Various Extraction Techniques of Curcumin—A Comprehensive Review." ACS Omega, 2023; 8: 1–20.

Traditional methods such as Soxhlet extraction, maceration, and solvent extraction were discussed along with advanced techniques including microwave-assisted extraction, ultrasound-assisted extraction, supercritical fluid extraction, and enzyme-assisted extraction. The review highlighted that advanced extraction methods improve curcumin yield, reduce solvent consumption, and minimize thermal degradation.

2.4. Saadati, S., et al. "Curcumin and Inflammation in Non-Alcoholic Fatty Liver Disease: A Randomized, Placebo-Controlled Clinical Trial."

Saadati et al. conducted a randomized placebo-controlled clinical trial to evaluate the effect of curcumin supplementation on inflammation in patients with Non-Alcoholic Fatty Liver Disease (NAFLD). The study aimed to determine whether curcumin could reduce inflammatory markers and improve liver function in affected individuals.

2.5. Yi, Q., et al. "A Critical Evaluation of Berberine in NAFLD Management: Recommendations for Improved Research Methodology."

Yi et al. critically evaluated the therapeutic role of berberine in the management of Non-Alcoholic Fatty Liver Disease (NAFLD). The review analyzed preclinical and clinical studies investigating the effects of berberine on lipid metabolism, insulin resistance, inflammation, and liver function.

2.6. Jeliński, T., Przybyłek, M., and Cysewski, P. "Natural Deep Eutectic Solvents as Agents for Improving Solubility, Stability and Delivery of Curcumin."

Jeliński et al. investigated the application of Natural Deep Eutectic Solvents (NADES) for improving the solubility, stability, and delivery of curcumin. The study highlighted the major pharmaceutical limitation of curcumin, namely poor aqueous solubility and low bioavailability.

2.7. Nassir, Fatiha, et al. "Pathogenesis and Prevention of Hepatic Steatosis." Gastroenterology & Hepatology, vol. 11, no. 3, 2015.

Nassir et al. discussed the pathogenesis, diagnosis, and prevention of hepatic steatosis, commonly referred to as Non-Alcoholic Fatty Liver Disease (NAFLD). The review explained that NAFLD is a metabolic liver disorder characterized by excessive fat accumulation in hepatocytes in individuals who consume little or no alcohol. It is strongly associated with obesity, insulin resistance, diabetes mellitus, dyslipidemia, and metabolic syndrome.

2.8. Peng, Cheng, et al. "Non-Alcoholic Steatohepatitis: A Review of Its Mechanism, Models and Medical Treatments."

Peng et al. reviewed the mechanisms, experimental models, and treatment approaches related to Non-Alcoholic Steatohepatitis (NASH), which represents the progressive inflammatory stage of NAFLD. The article described NASH as a condition characterized by hepatic fat accumulation accompanied by inflammation, hepatocellular injury, and varying degrees of fibrosis.

The study concluded that NASH is a complex multifactorial disease requiring early diagnosis and combination therapeutic approaches to prevent progression toward fibrosis and cirrhosis. Fibrosis: Persistent Inflammation Leaves the Surrounding Blood Vessels and Liver Tissue Scarred Fibrosis represents the third stage in the progression of Non-Alcoholic Fatty Liver Disease, where persistent inflammation and hepatocellular injury lead to excessive deposition of extracellular matrix proteins and scar tissue formation in the liver. Although liver function remains partially preserved during this stage, continuous injury may progress to irreversible cirrhosis and liver failure if left untreated.

2.9. Amaroli, Andrea, et al. "The Bright Side of Curcumin: A Narrative Review of Its Therapeutic Potential in Cancer Management." Cancers, vol. 16, no. 14, 2024, p. 2580. MDPI AG

This study utilizes a quantitative bibliometric approach to map the global landscape of berberine research from 1985 to 2018, tracking publication outputs, prominent institutional contributors, and shifts in research direction. The analysis reveals that berberine research has transitioned from localized, traditional studies into a massive global pharmacotherapy interest.

2.10. Gao, Yu, et al. "The status of and trends in the pharmacology of berberine: a bibliometric review [1985– 2018]." Chinese Medicine, vol. 15, 2020, p. 15. Springer Science and Business Media LLC

This study utilizes a quantitative bibliometric approach to map the global landscape of berberine research from 1985 to 2018, tracking publication outputs, prominent institutional contributors, and shifts in research direction. The analysis reveals that berberine research has transitioned from localized, traditional studies into a massive global pharmacotherapy interest.

2.11. Habtemariam, Solomon. "The Quest to Enhance the Efficacy of Berberine for Type-2 Diabetes and Associated Diseases: Physicochemical Modification Approaches." Biomedicines, vol. 8, no. 4, 2020, p. 90. MDPIA

The authors detail the primary botanical families rich in berberine—such as Berberidaceae and Ranunculaceae— and document its widespread use in folk medicine across Asian and Native American cultures. The core of the review focuses on characterizing its broad-spectrum pharmacological activities. It compiles substantial evidence supporting berberine's efficacy as a potent anti-inflammatory, antioxidant, and antimicrobial agent capable of combating diverse pathogens, including antibiotic-resistant bacterial strains.

2.12. Singh, N., et al. "Intrinsic medicinal qualities and current status of curcumin." International Journal of Pharmaceutics & Drug Analysis, vol. 3, no. 1, 2015, pp. 11-15. The paper emphasizes the basic, highly versatile healing properties of curcumin that have made it a staple of traditional Indian Ayurveda. It details its efficacy in accelerating wound healing, reducing systemic inflammation, alleviating pain (nociceptive properties), and acting as an anti-parasitic agent. The authors outline its early clinical trials, noting that while its safety profile is remarkably high even at massive doses, its therapeutic impact is consistently restricted by rapid metabolism and elimination.

2.13. Turmeric: A Comprehensive Review of Its Botany, Traditional Uses, Phytochemistry, and Mechanisms as a Functional Food." Nutrients, vol. 18, no. 8, 2026, p. 1197.

This high-impact review evaluates whole turmeric as a functional food, moving beyond just isolated curcumin to analyze the synergistic interaction of its complete phytochemistry (including essential oils and non-curcuminoid compounds).The review comprehensively details how turmeric targets fundamental molecular pathways, specifically downregulating major inflammatory drivers like nuclear factor-κB (NF-κB) and cyclooxygenase-2 (COX-2).

Furthermore, it introduces exciting modern data regarding turmeric's role in epigenetics. It highlights how the active compounds in turmeric can influence DNA methylation and histone acetylation, effectively turning off pro-inflammatory genes and reactivating tumor-suppressor genes to halt cancer progression.

2.14. Joshi, Naresh Dilip, et al. "Extraction of Curcumin from Turmeric by Using Soxhalet Unit." ASIO Journal of Microbiology, Food Science & Biotechnological Innovations (ASIO-JMFSBI), 2019; 4(1): 11–14.

The researchers demonstrate the practical execution of the Soxhlet process, examining how variables such as solvent selection and cycle duration impact the final purity and yield of extracted curcuminoids. The study confirms that the continuous refluxing nature of the Soxhlet unit prevents the saturation boundaries common in static extractions, allowing the solvent to thoroughly penetrate the cellular structures of the turmeric powder.

2.15. Hussain, Ghulam. "Soxhlet Extraction: Principle, Working & Usage." Punjab Oil Mills Limited, July 2023

This industrial white paper establishes the theoretical framework, operational mechanics, and broad industrial applications of the Soxhlet extraction.

3. AIM AND OBJECTIVES

Aim: To formulate and evaluate a multinutrient capsule containing Berberine and Curcumin for the supportive management of NAFLD/MASLD.

Objectives

1. To prepare a herbal capsule formulation using Berberine and Curcumin.
2. To study the physical and preformulation properties of the ingredients used in the formulation.
3. To check the compatibility between the drugs and excipients used in the capsule.
4. To improve the solubility and absorption of the formulation for better effectiveness.
5. To evaluate the prepared capsules for quality parameters such as:

- weight variation,
- disintegration time,
- drug content,
- drug release profile.

6. To study the antioxidant and liver-protective effects of the formulation.

4. PLAN OF WORK

Literature review
Selection and Procurement of Materials
Preformulation Studies
Formulation Development
Evaluation Of Capsules
Stability Study
Data Analysis And Interpretation
Result and Discussion
Conclusion
Future Scope

5. DRUG PROFILE

5.1 BERBERINE

Synonyms: Berberine hydrochloride, Umbellatine, Natural isoquinoline alkaloid

Biological Source

Berberine is a quaternary isoquinoline alkaloid obtained from the roots, rhizomes, bark, and stems of plants such as Berberis vulgaris (Barberry), Coptis chinensis (Goldthread), and Berberis aristata belonging to family Berberidaceae.

5.1.1 Taxonomical Classification of Berberis vulgaris

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Ranunculales

Family: Berberidaceae

Genus: Berberis

Species: Berberis vulgaris

Fig.no. 6.1.

5.1.2 Chemical constituent

Berberine is the major bioactive alkaloid present in barberry species. It also contains several related alkaloids and phenolic compounds.

1. Alkaloids -Berberine, Palmatine, Jatrorrhizine, Columbamine
2. Phenolic compounds -Phenolic acids, tannins
3. Flavonoids- Quercetin, rutin
4. Organic acids- Malic acid, citric acid
5. Vitamins-Vitamin C
6. Minerals- Calcium, potassium, magnesium

5.1.3 Pharmacological Activity of Berberine

5.1.3.1 Anti microbial activity

5.1.3.2 Anti Fungal activity

5.1.3.3 Anti oxidant activity

5.1.3.4 Anti inflammatory activity

5.1.3.5 Anti diabetic activity

5.1.3.6 Hepatoprotective activity

5.1.3.7 Anti cancer activity

5.1.4 Uses

1. Lower blood sugar level
2. Improve cholesterol level
3. Support weight management
4. Aid gut health
5. PCOS support[27][28][29]

5.2 CURCUMIN

5.2.1 Curcumin(Curcuma longa)

5.2.2 Synonyms: Turmeric, Haldi, Haridra, Indian saffron

Biological Source

Curcumin is the principal curcuminoid obtained from the dried rhizomes of Curcuma longa Linn. belonging to family Zingiberaceae.

5.2.3 Taxonomical Classification of Curcuma longa

Kingdom: Plantae

Division: Magnoliophyta

Class: Liliopsida

Order: Zingiberales

Family: Zingiberaceae

Genus: Curcuma

Species: Curcuma longa

5.2.4 Chemical constituent

1. Curcuminoids-Curcumin, Demethoxycurcumin, Bisdemethoxycurcumin
2. Volatile oils-Turmerone, Atlantone, Zingiberene
3. Proteins-Albumins and globulins
4. Carbohydrates-Starch
5. Vitamins-Vitamin C, Vitamin E
6. Minerals-Iron, potassium, manganese
7. Phenolic compounds-Ferulic acid, caffeic acid

Fig.no. 6.2.

5.2.5 Pharmacological Activity of Curcumin

- Anti oxidant activity
- Anti microbial activity
- Wound healing activity
- Anti cancer activity
- Hepatoprotective activity
- Immunomodulatory activity

5.2.6 Uses

1. Brain health support

2. Anti inflammatory activity
3. Support liver health
4. Improve digesion[30][31]

6. METHODOLOGY

Table no 6.1 Ingredients used in study.

SR NO.	INGREDIENTS	SUPPLIED BY	CATEGORY
1.	Curcumin	Sunpure pharma	API
2.	Berberine	Sunpure pharma	API
3..	Piperine	HIMEDIA	Bioavailability enhancer
4.	MCC	Eisen Golden Laboratories	Diluent
5.	Talc	Chemicalstore.com	Glidant
6.	Magnesium Stereate	Chemicalstore.com	Lubricant

Table no 6.2 Instruments used in study.

SR NO.	NAME OF INSTRUMENT	MAKE/MODEL
1.	Digital weighing balance	Contech
2.	Ph Meter	Electro Lab
3.	Capsule filling machine	AVain Labs
4.	Manual capsule filling tray	AVain Labs
5.	Ultrasonic cleaner (Sonicator)	PS-10A
6.	UV Spectrophotometer	SHIMADZU
7.	Capsule dissolution apparatus	Labindia instruments
8.	Capsule disintegration apparatus	Labindia instruments
9.	Hot air Oven	Lab solution india

6.1. Equipments and apparatus

- Laboratory Balance or Digital weighing scale
- Mortar and Pestle for Grinding and powdering the ingredients.
- Sieve or mesh strainer for removing any coarse particle.
- Spatula for mixing.
- Soxhlet apparatus for extraction purpose.
- Reflux condenser.
- Funnel for transferring the extraction to containers and for flow property analysis.
- Grinder for grinding the ingredients.
- Air tight container for storage.
- Beaker and conical flask.
- Oven for drying of API.
- Seperating funnel.-

- Standard sieves and sieve shaker for size separation.
- Magnetic stirrer.
- Disintegration test apparatus for disintegration.
- Dissolution test apparatus.
- Polyethene bags.
- Whatman Filter paper.
- Ph meter.
- Water bath

It is important to ensure that all materials and equipments used are clean and free from any contaminants to maintain the quality and effectiveness of NAFLD herbal capsule. Proper labelling and storage of containers will help in easy identification and preservation of powder. Additionally, following good 24 laboratories practices and safety guidelines is essential to ensire a safe and hygienic preparation process.

6.2. Exepients profile

6.2.1. Piperine

- **Trade name -** Bioperine
- **Chemical name** - 1-piperoylpiperidine
- **Molecular weight -** 285.34gm
- **Chemical formula -** C17H19NO3
- **Structure**

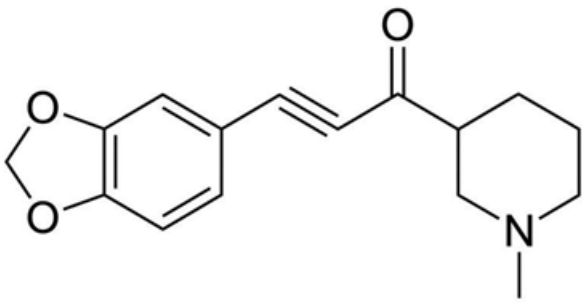


Fig.no. 6.1.

- **Appearance –** Black colour crystalline powder
- **Density –** 1.193 gm/ cm³
- **Refractive Index-** 1.6846 (measured at 20°**C)**

- **pH-** Weakly basic (12.22)
- **Application of formulation –** For enhancing the absorption of the drug.

6.2.2. MCC

- **Trade name:** Avicel PH 101, Avicel PH 102
- **Chemical name:** Microcrystalline cellulose
- **Molecular weight**: 36,000 g/mol
- **Chemical Formula**: (C6H10O5)n
- Structure:

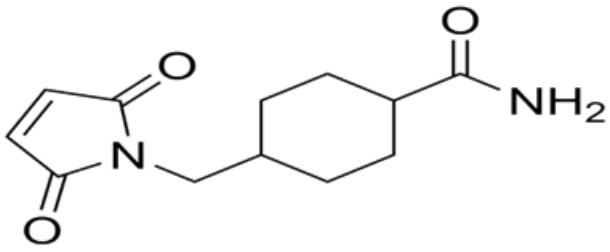


Fig.no. 6.2.

- **Appearance:** White, odourless, tasteless, crystalline powder.
- **Density:** Approximately 1.5-1.6g/cm3
- **Refractive Index**: 1.530
- **PH:** 5.0-7.5
- **Melting Point:** Decomposes at approximately 265 **°C**.
- Functional Role in research formulation.
- Microcrystalline cellulose was used as a diluent, binder, and disintegrating agent in the capsule/tablet formulation. It improves powder flow properties, enhances compressibility, and preparation. MCC also contributes to better mechanical strength and rapid disintegration of the formulation.[33][34][35]

6.2.3. Magnesium Stearate

- **Trade name:** Ligamed MF-2-V
- **Chemical name:** Magnesium Octadenoate
- **Chemical formula:** Mg(C18H35O2)2
- **Molecular weight:** 591.24g/mol

- Structure:

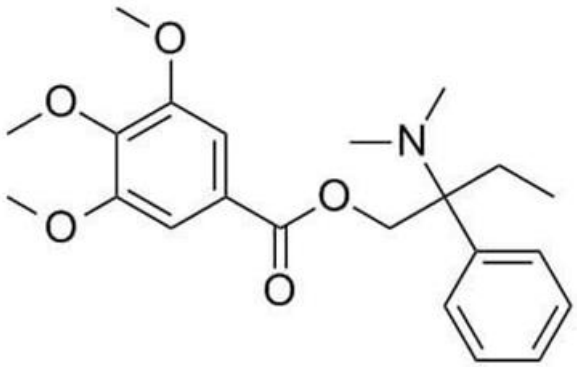


Fig.no.6.3.

- **Appearance:** Fine, white, light powder with characteristic odour.
- **Density:** Approximately 1.03 g/cm2
- Refractive index: **1.55**
- **pH:** 7.0-8.5
- **Melting point:** 117-150°C
- **Functional role:** magnesium stearate was incorporated as a lubricant and anti-adherent in the formulation. It minimizes friction during capsule filling or tablet compression, prevents sticking to equipment surfaces, and improves manufacturing efficiency and flow characteristics of the blend.[34][37][36]

6.2.4. Talc

- **Trade name:** Purified talc
- **Chemical name:** Hydrated Magnesium Silicate
- **Chemical formula:** Mg3Si4O10(OH)2
- **Molecular weight:** 379.29 g/mol
- Structure:

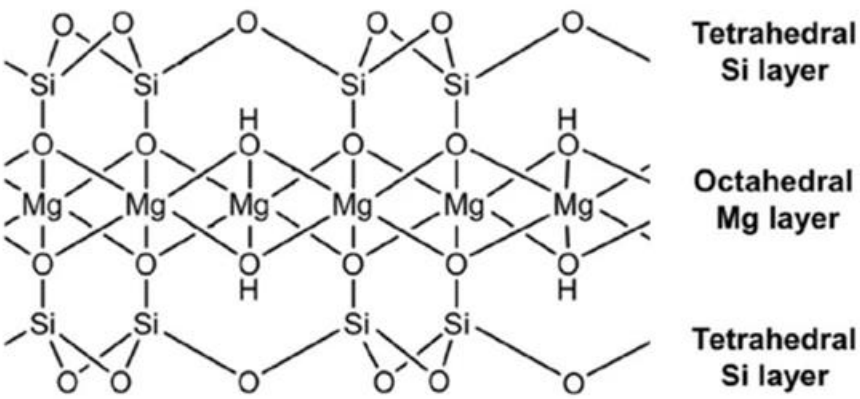


Fig.no.6.4.

- **Appearance:** Very fine, white to greyish-white powder.
- **Density:** 2.7-2.8 g/cm^3
- **Refractive index:** 1.54-1.59
- **pH:** 7-9
- **Melting point:** Approximately 1500°C
- **Functional role in research formulation:** Talc was used as a glidant and lubrication in the formulation to improve powder flowability and reduce inter-particle friction during processing. It also helps in preventing sticking during compression and enhances uniform filling of capsules.[34][38][39]

6.3. Method of extraction

6.3.1. Principle of Soxhlet extraction: The Soxhlet extraction method uses a small amount of solvent and is very cost- effective. The Soxhlet extraction uses the solvent reflux and siphon principle to continuously extract the solid matter by pure solvent, which saves the solvent extraction efficiency and high efficiency. The sold sample is placed on a thimble-shaped filter paper, positioned into Soxhlet extractor, and the device is assembled. The solvent is added to the solvent reservoir flask and mounted onto a heating mantle. After heating, the condensed vapours of the solvent come in contact with the sample powder, and the soluble part of the powder gets mixed with the solvent for extraction. When the solvent surface exceeds the maximum height of the siphon, the solvent containing the extract is siphoned back. The flask is repeated, extracting a portion of the material each time so that the solid material is constantly used as a pure solvent and the extracted material is concentrated in the flask.

6.3.2. Soxhlet extraction procedure for Curcumin

Soxhlet extraction is a highly effective, continuous technique used to isolate curcumin from turmeric. It works by repeatedly cycling a hot, vaporized solvent through a thimble of ground turmeric. This continuously washes and dissolves the curcuminoids into the solvent, maximizing the extraction yield.

6.3.2.1. Materials Needed

Raw material: High-quality dried turmeric rhizome powder. Chemical constituents: 75% Ethanol.

Equipment: Soxhlet apparatus (round-bottom flask, extractor, condenser), cellulose thimble, heating mantle, and a rotary evaporator

6.3.2.2. Procedure

1. Sample Preparation: Clean fresh turmeric rhizomes and dry them in the hot air oven at 50°C until brittle. Grind the dried rhizomes into a fine, uniform powder using a mortar and pestle.
2. Assembly and Loading: Weigh 10 g of the dried turmeric powder and place it evenly into a cellulose extraction thimble. Insert the thimble into the main chamber of the Soxhlet extractor.
3. Solvent Addition: Pour approximately 250 mL of your chosen solvent (ethanol) into the round-bottom flask. Attach the flask to the extractor and place the condenser on top.
4. Extraction Process: Place the round-bottom flask in a heating mantle. Set the temperature to the boiling point of the solvent (78.37°C). Allow the apparatus to run continuously for 6 to 8 hours until the solvent in the extractor siphon tube becomes clear and colourless.
5. Solvent Recovery and Yield: Once the extraction is complete, disconnect the apparatus, use a vacuum rotary evaporator at approximately 40°C-45°C to remove the solvent from the liquid extract. The result is dark-orange residue in the flask which is crude curcumin extract.

6.3.2.3. Soxhlet extraction of berberine

Soxhlet extraction of berberine involves using a solid-liquid continuous extraction method with 75% aqueous ethanol as the solvent. This technique circulates hot, condensed solvent through a sample of dried botanical material (barberry root) to dissolve and isolate the active alkaloid.

6.3.2.4. Materials Needed

Raw Material: Finely ground dried root of berberine of Berberis vulgaris. Solvent: 75% ethanol.

Equipment: Soxhlet extractor assembly (round-bottom flask, thimble holder, extractor, and condenser), cellulose extraction thimbles, and a heating mantle.

Post-Extraction: Rotary evaporator.

6.3.2.5. Procedure

1. Sample Preparation: Accurately weigh 10g powdered plant material. Place the powder inside a porous cellulose extraction thimble.
2. Apparatus Assembly: Place a few anti-bumping boiling chips into the round-bottom flask and add the 75% ethanol solvent,. insert the loaded thimble into the main Soxhlet chamber Attach the round-bottom flask to the bottom of the extractor and the condenser to the top.
3. Extraction Process: Turn on the heating mantle and the condenser cooling water. Heat the solvent to a boiling point (78.37°C). The solvent will vaporize, travel up the vapour tube, condense, and drip into the thimble to extract the berberine. Once the extraction chamber fills, it will siphon the berberine-rich solvent back into the round-bottom flask. Allow the cycle to repeat continuously for roughly 6 to 8 hours until the siphoning solvent appears clear and colourless.

Concentration: Remove the extract, detach the round-bottom flask, and use a rotary evaporator to distil off the ethanol under a vacuum. This leaves a concentrated, berberine-rich crude extract.[40],[41],[42]

Table no. 6.3: Formulation Batches.

Sr.no.	API/Excipients	Batch F1	Batch F2	Batch F3
1.	Curcumin	172 mg	172 mg	172 mg
2.	Berberine	137 mg	137 mg	137 mg
3.	Talc	4 mg	4 mg	6 mg
4.	Piperine	7 mg	7 mg	6 mg
5.	MCC	25 mg	27 mg	24 mg
6.	Magnesium stearate	5 mg	3 mg	5 mg

7. RESULTS AND DISCUSSION

Appearance

Table no 7.1 Appearance.

Sr no.	Formulation	Physical, Appearance
1.	F1	Bright Yellow to Yellow orange
2.	F2	Bright yellow to yellow orange
3.	F3	Bright yellow to yellow orange

Bulk Density

The bulk density of all herbal capsule powder formulations was determined to evaluate the packing ability and flow property of the powder blend. The bulk density values indicated good packing characteristics suitable for capsule filling.

Table no. 7.2: Bulk Density.

Sr. no.	Formulation	Bulk Density (g/ml)
1.	F1	0.31
2.	F2	0.43
3.	F3	0.35

Tapped Density

The tapped density of all formulations was determined for evaluation of flow characteristics and compressibility behaviour of the herbal powder blend. The results showed acceptable tapped density values for capsule formulation.

Table no. 7.3: Tapped Density.

Sr. no.	Formulation	Tapped Density (g/ml)
1.	F1	0.41
2.	F2	0.49
3.	F3	0.44

Carr's Index

Carr's index was determined to evaluate the compressibility and flow properties of the herbal capsule p[owde blend. All formulations showed acceptable Carr's index values indicating good flow characteristics. Comparitively, formulation F3 showed better flow properly among all formulations.

Table no. 7.4: Carr's Index.

Sr. no.	Formulation	Carr's Index (%)
1.	F1	24%
2.	F2	12%
3.	F3	20%

Hausner ratio

Hausner ratio was evaluated to determine the flowability of the herbal capsule powder formulations. All formulations showed Hausner ratio values within acceptable limits indicating good flow property suitable for capsule filling.

Table no. 7.5: Hausner's Ratio.

Sr. no.	Formulation	Hausner Ratio
1.	F1	1.35
2.	F2	1.13
3.	F3	1.25

Angle of Repose

The angle of repose was determined to evaluate the flowability of the herbal powder blend used for capsule formulations. All formulations showed angle of repose values below30°, indicating good flow characteristics. Formulation F3 showed comparatively better flow property than formulations.

Table no. 7.6: Angle of Repose.

Sr. no.	Formulation	Angle of Repose
1.	F1	32.0
2.	F2	33.7
3.	F3	31.4

Moisture content/Loss on drying (LOD)

The loss on drying test was performed to determined the moisture content present in the herbal capsule formulations. The moisture content of all formulations was found within acceptable limits, indicating good stability and low risk of microbial growth in the formulation.

Table no. 7.7: LOD.

Sr. no.	Formulation	LOD (%)
1.	F1	2.76%
2.	F2	2.8%
3.	F3	2.77%

pH determination

The pH of all herbal formulations range 6-6.5 from which is appropriate for the stomach and liver making the compatibility of the herbal capsules formulation with the gut.

Table no. 7.8: pH Determination.

Sr no.	Formulation	pH
1.	F1	6.1
2.	F2	6.4
3.	F3	5.9

Weight Variation

The weight variation test was performed to ensure uniformity of capsule weight in all herbal capsule formulation. 20 capsules from each formulation were weigh individually and the average weight was calculated. All formulation were found within the acceptable pharmacopial limits, indicating uniform filling if the capsule powder blend.

Table no. 7.9 Weight Variation.

Sr no.	Formulation	Weight variation
1.	F1	Pass
2.	F2	Pass
3.	F3	Pass

Disintegration

The disintegration test was performed to determine the time required for the herbal capsule formulation to disintegrate completely in specific medium. The test was carried out using 0.1N HCL maintain at 37°C. All formulations were found to disintegrate within the acceptable pharmacopeia limit for hard vegetarian capsule, indicating suitable release characteristics of the formulations.

Table no. 7.10: Disintegration.

Sr no.	Formulation	Disintegration time
1.	F1	7.2
2.	F2	9.7
3.	F3	9

Dissolution Study

The dissolution study was performed to evaluate the drug release profile of the herbal capsule formulation. The test was carried out using USP type II dissolution apparatus containing 900ml 0.1N HCL maintain at 37°C and operate at 75 rpm. All formulation showed satisfactory drug release within the specific time, indicating proper dissolution characteristics of the herbal capsule formulation.

Table no. 7.11 Dissolution study.

Sr. no.	Formulation	Drug Release (%)
1.	F1	82%
2.	F2	98%
3.	F3	87%

Drug Content

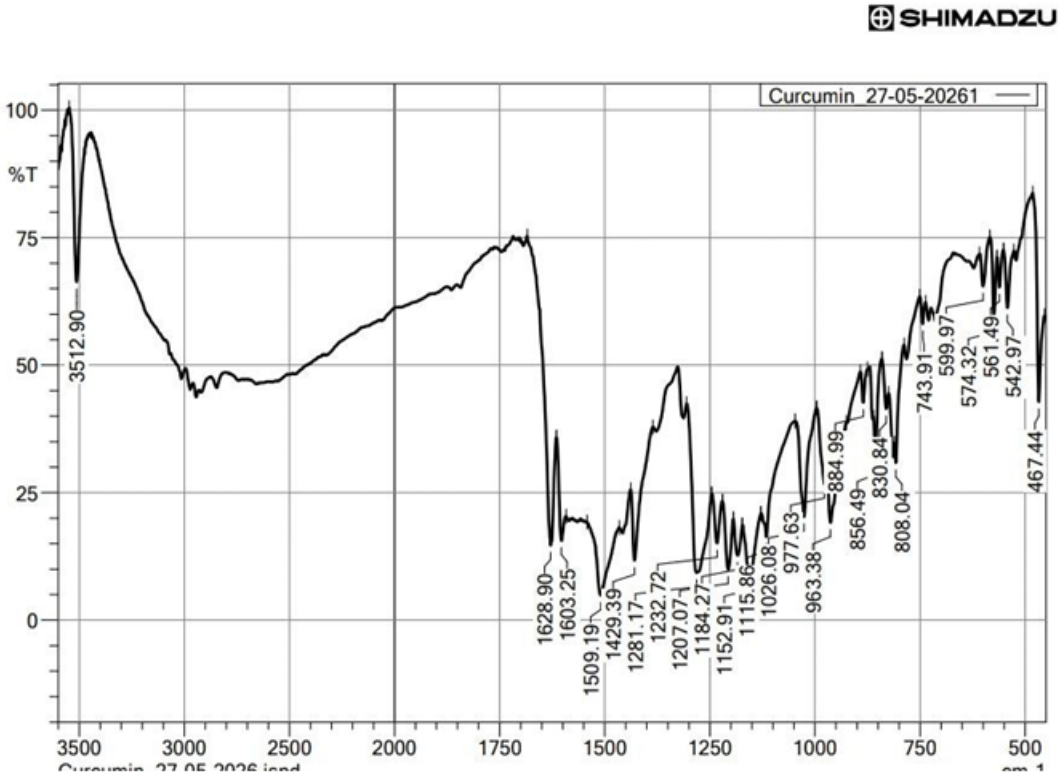
The drug content assay of the herbal capsule formulation was determined using UV spectrophotometric analysis. The λ max of curcumin was found in range of 420-430nm, while berberine showed λ max around 345nm. A calibration curve was prepared and the drug content of all formulation was evaluated. The results indicated uniform distribution of the active constituents within the acceptable limits.

Table no. 7.12: Drug Content.

Sr. no.	Formulation	Drug Content (%)
1.	F1	96.8%
2.	F2	98.2%
3.	F3	94.5%

Fourier-Transform Infrared Spectroscopy

Fourier-Transform Infrared Spectroscopy (FTIR) is a versatile analytical technique used to identify organic, polymeric, and select inorganic materials. The method operates by passing infrared radiation through a sample and measuring the specific wavelengths absorbed by the chemical bonds. Each molecule produces a unique spectral fingerprint based on its functional groups, allowing for precise material identification. Modern FTIR spectrometers utilize an interferometer to collect data across all frequencies simultaneously, which a Fourier-transform algorithm then converts into a readable spectrum. This process offers high sensitivity, exceptional speed, and minimal sample preparation compared to older dispersive methods. Consequently, the technique is widely applied in quality control, environmental monitoring, pharmaceutical analysis, and forensic science to detect impurities and verify compound structures.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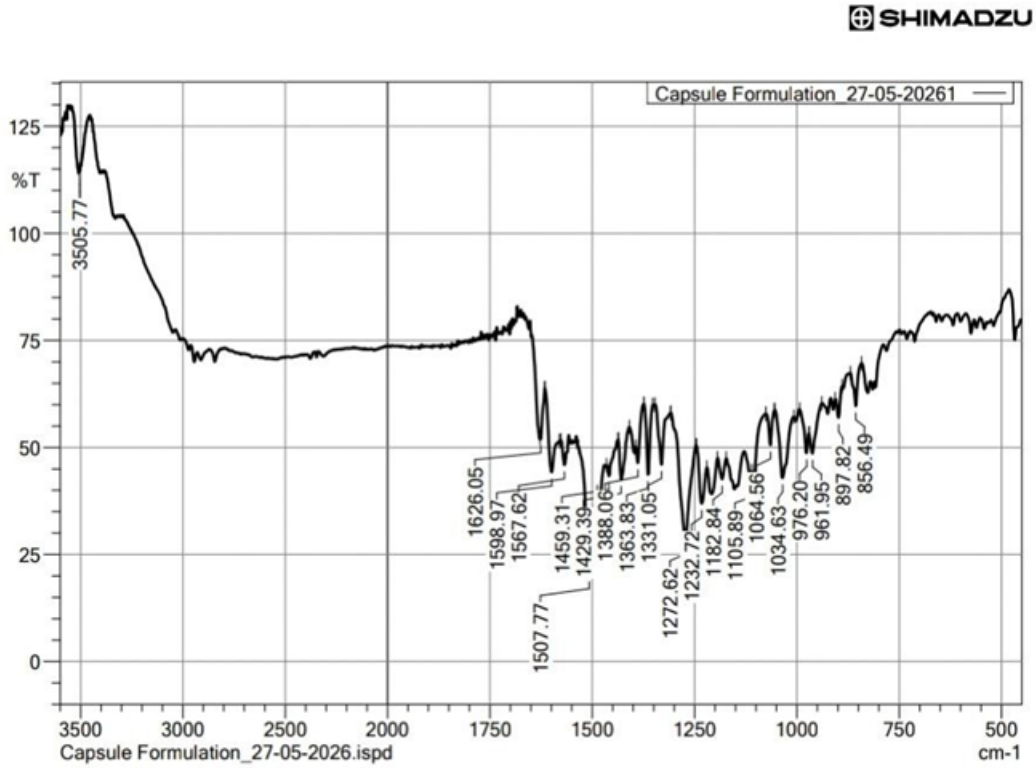
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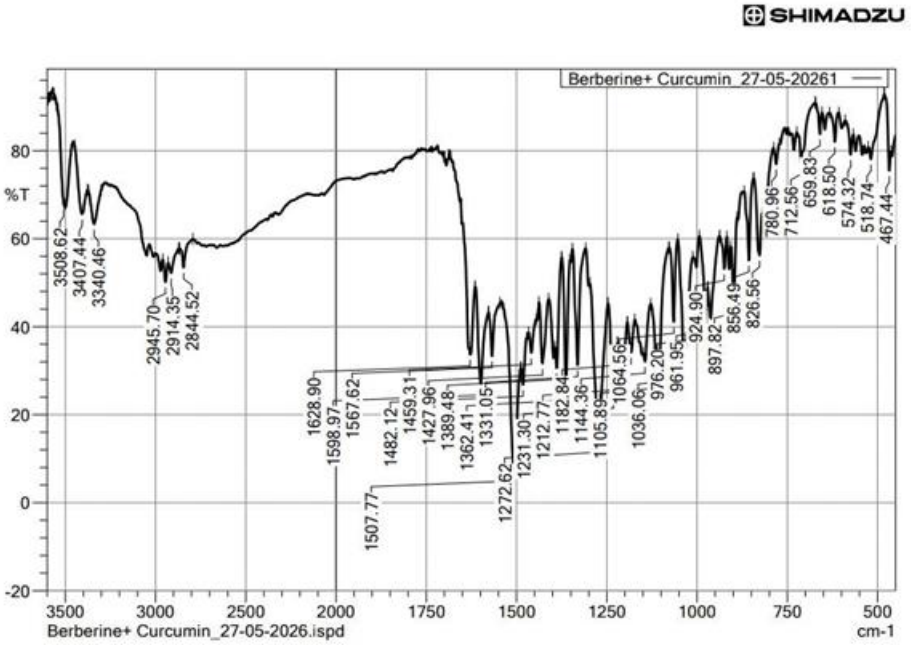

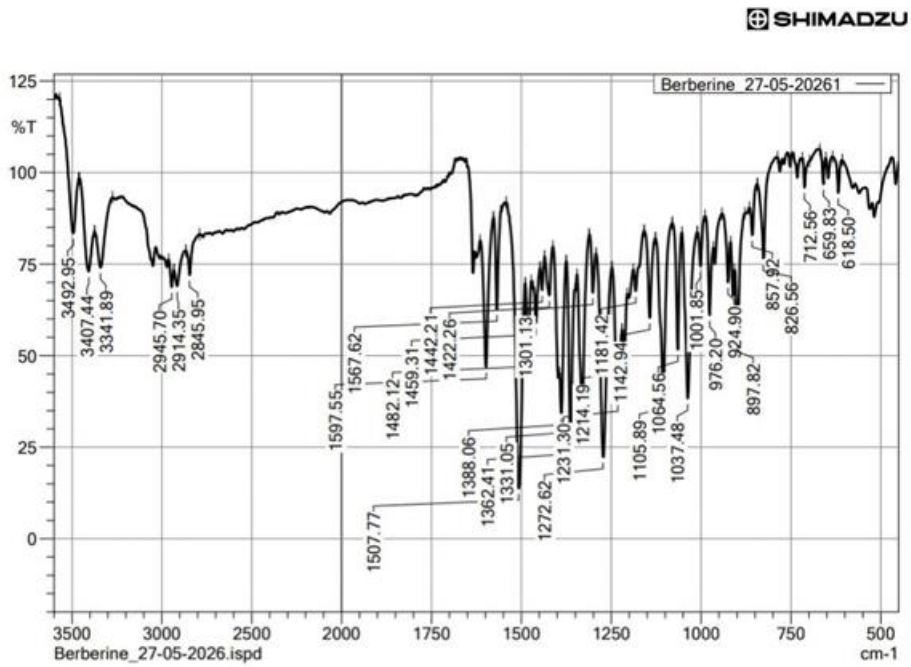

8. CONCLUSION

In the present study, we successfully formulated and evaluated a nutraceutical capsule containing Berberine and Curcumin for the supportive management of Non-Alcoholic Fatty Liver Disease (NAFLD). The formulation was developed with the objective of utilizing the hepatoprotective, antioxidant, anti-inflammatory, and lipid-lowering properties of both natural compounds to provide a safer and effective therapeutic approach. The prepared capsules were evaluated for various preformulation and postformulation parameters such as flow properties,

weight variation, disintegration time, and drug content, and the results obtained were found to be within acceptable limits. UV-visible spectrophotometric analysis confirmed the presence and estimation of berberine and curcumin at their respective wavelengths. Based on the overall findings, the formulated nutraceutical capsules demonstrated satisfactory pharmaceutical characteristics and showed potential for improving liver health by reducing oxidative stress, inflammation, and hepatic lipid accumulation associated with NAFLD. The combination of berberine and curcumin may provide synergistic therapeutic benefits and could serve as a promising supportive therapy for fatty liver management. Further studies such as in-vitro, in-vivo, and clinical investigations are recommended to establish the long-term efficacy, safety, and therapeutic potential of the developed formulation.

9. FUTURE PERSPECTIVE

Non-Alcoholic Fatty Liver Disease (NAFLD) has become a common health concern in recent years due to changes in lifestyle, unhealthy food habits, and lack of physical activity. As the number of cases continues to rise, there is a growing need for treatment options that are effective and safe for long-term use. Herbal medicines are receiving more attention because they are natural in origin and are generally considered suitable for prolonged use. The present study on the formulation and evaluation of herbal capsules containing berberine and curcumin showed encouraging results and provides a strong base for further research in this area. In the future, this research can be extended through animal studies and clinical trials on human subjects to understand the effectiveness of the formulation in a better way. These studies can help evaluate how the formulation performs over a longer period and whether it supports improvement in liver health in patients with NAFLD. Clinical studies can also help in deciding the most suitable dose and duration of treatment for better results. Another important area for future work is improving the formulation itself. Berberine and curcumin are known for their beneficial effects, but their absorption in the body can sometimes be limited. More advanced formulation techniques may be used in future to improve their absorption and overall effectiveness. This may help increase the therapeutic value of the capsules and make the formulation more beneficial. Further studies may also focus on related health conditions commonly associated with NAFLD, such as obesity, high cholesterol, and insulin resistance. Since berberine and curcumin are reported to have antioxidant and anti-inflammatory properties, there is a possibility that this formulation may offer additional health benefits apart from liver support. Studying these effects can provide a wider understanding of its potential uses. Standardization of herbal ingredients will also remain important in future development.

Maintaining the quality, purity, and consistency of the raw materials and final formulation is necessary for reliable results. Advanced analytical techniques and stability studies can be carried out further to confirm the quality of the capsules and their performance during storage. This can also be useful if the formulation is developed on a larger scale. There is also increasing interest among people in herbal and plant-based healthcare products. Because of this, formulations like the present herbal capsule may have a good future in both pharmaceutical and nutraceutical fields. With further scientific validation and proper approval, it may become a useful supportive option for managing fatty liver and promoting better liver health. Overall, the present study offers a valuable starting point for future research. With additional investigation and development, this herbal formulation containing berberine and curcumin may contribute as a beneficial and natural supportive approach in the management of NAFLD.

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