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Research Article

Clinical Evaluation of an Herbal-Probiotic Nutraceutical Supplement in Improving Symptoms of *Yakrut Vikaara, Kaamala*, and *Pleeha Roha*: A Pilot Clinical Study

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ABSTRACT

The liver, as the body's primary detoxification organ, is highly vulnerable to toxins such as heavy metals, pesticides, industrial chemicals, and alcohol. These substances can cause oxidative stress, inflammation, and liver cell damage, potentially leading to fatty liver disease like the development of non-alcoholic fatty liver disease (NAFLD), cirrhosis, or liver cancer. Environmental pollutants from air and water further contribute to liver dysfunction by overwhelming detoxification pathways and promoting chronic metabolic disturbances. Herbal and probiotic-based nutraceuticals have shown promise in supporting detoxification and improving digestive health. This pilot study evaluated the safety and efficacy of a novel nutraceutical supplement formulated with six herbs and a probiotic in patients with liver disorders, hepatitis, and spleen-related disorders exceeding 30% of the population in Salem city, India. **Methods:** In a Phase I, single-centre, open-label clinical trial, 10 patients (40% female, 60% male) diagnosed with liver and spleen disorders presenting symptoms including excessive tiredness, shortness of breath, loss of appetite, nausea, abdominal pain, fatigue, and bloating were administered the supplement. Symptom improvement was assessed over the study period. **Results:** The nutraceutical demonstrated a high level of tolerability among participants, with no significant adverse effects reported. Notably, 80% of the patients experienced noticeable improvements across a broad range of symptoms. These positive outcomes suggest that the product may offer beneficial effects in several key areas, including the body's natural detoxification processes, digestive function, and the maintenance of overall health and well-being. These findings highlight the potential of the nutraceutical as a supportive supplement for individuals seeking to enhance their physiological balance and general vitality. **Conclusion:** This pilot study suggests that the six-herb probiotic nutraceutical supplement may offer symptomatic relief and support detoxification in patients with liver and spleen disorders. Larger, controlled studies are warranted to confirm these findings.

INTRODUCTION

Metabolic toxicity refers to the harmful effects of substances that disrupt normal metabolic processes in the body, particularly those that impact cellular function and organ systems. Environmental toxins, such as heavy metals, industrial chemicals, pesticides, and certain food additives, can accumulate in the body and cause significant damage to liver health. The liver, being a primary detoxification organ, is especially vulnerable to these toxins. For instance, substances like alcohol, methanol, and

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synthetic chemicals can cause oxidative stress, inflammation, and liver cell damage. Over time, this exposure may lead to conditions such as fatty liver disease, cirrhosis, or even liver cancer. In addition to these chemical exposures, environmental pollutants like air and water toxins contribute to liver dysfunction by overwhelming the body's detoxifying capacity, leading to chronic toxicity and metabolic disturbances (Ala et al., 2006; Wahlang et al., 2019; Zheng et al., 2021 and Nguyen et al., 2022). Methanol occurs naturally in small amounts in certain fresh produce, such as fruits and vegetables, as well as in fermented beverages. In addition to these dietary sources, methanol is also found in a variety of industrial and household products, including cleaning agents, methylated spirits, fungicides, insecticides. Once ingested, methanol is absorbed into the bloodstream and transported to the liver, where it undergoes enzymatic metabolism to formaldehyde and subsequently to formic acid. Accumulation of formic acid can lead to metabolic acidosis, a condition that disrupts the body's acid–base balance. This acidotic state may contribute to histotoxic hypoxia and lactic acidosis, both of which impair cellular respiration and energy metabolism (Skrzydlewska 2003). Beyond dietary sources, occupational exposure to industrial chemicals represents another major pathway for chronic liver toxicity. The study conducted by Tovoli et al. has established a clear link between occupational exposure and the increased risk of liver cirrhosis and cancer. The hypothesis was proved with a trial for individuals with Metabolic dysfunction-associated steatotic liver disease (MASLD) categorised into two groups depending on their health conditions and complications like Advanced Chronic Liver Disease (ACLD) and Hepatocellular Carcinoma (HCC) and lifestyle habits. It was determined that a long-term exposure to toxicants could be one of the main reasons for severe MASLD (including ASLD and HCC). The toxicant exposures investigated in this study encompassed a broad range of chemical agents and industrial emissions. These included heavy metals such as arsenic, beryllium, cadmium, copper, lead, thallium, and selenium; solvents including carbon tetrachloride, dichloromethane, dichloropropane, dichloropropanol, dimethylacetamide, dimethyl formamide, dioxane, nitropropane, styrene, tetrachloroethylene, trichloroethylene, trichloroe thane, tetrachloromethane, trichloro propane, and trifluorodichloroethane; and industrial chemicals such as vinyl chloride and halogenated refrigerants. Additional exposures comprised of ethanol, carbon disulphide, dioxins, phosphorus, pesticides, insecticides, and explosives including picric acid and trinitrotoluene. The study also considered occupational contact with colourants, paints, pigments, resins, plastic industry emissions, synthetic rubber production by-products, fuel emissions, and laboratory reagents such as chloronaphthalene and tetrabromomethane (Tovoli et al., 2024).

Epidemiological and toxicological studies have identified positive associations between environmental contaminants such as microcystins (MCs), disinfection by-products (DBPs), heavy metals (HMs), dioxins, and polychlorinated biphenyls (PCBs) and the development of non-alcoholic fatty liver disease (NAFLD) (Zheng et al., 2021). A recent study conducted by Costello et al. provides compelling evidence that endocrine-disrupting chemicals (EDCs) can induce metabolic changes that contribute to the development of non-alcoholic fatty liver disease (NAFLD). This hypothesis is supported by both human meta-analyses and complementary animal studies. In particular, per and polyfluoroalkyl substances (PFAS)—a class of 'forever chemicals' named for their strong carbon–fluorine bonds and resistance to metabolic and environmental degradation—have been implicated. Human biomonitoring studies have detected PFAS in the blood of the majority of the U.S. population, underscoring the widespread nature of exposure. PFAS exposure has been associated with elevated levels of liver enzymes, notably alanine aminotransferase (ALT), formerly known as serum glutamate pyruvate transaminase (SGPT). Elevated ALT levels are indicative of liver injury and suggest a potential link between PFAS and liver damage. (Costello et al., 2022)

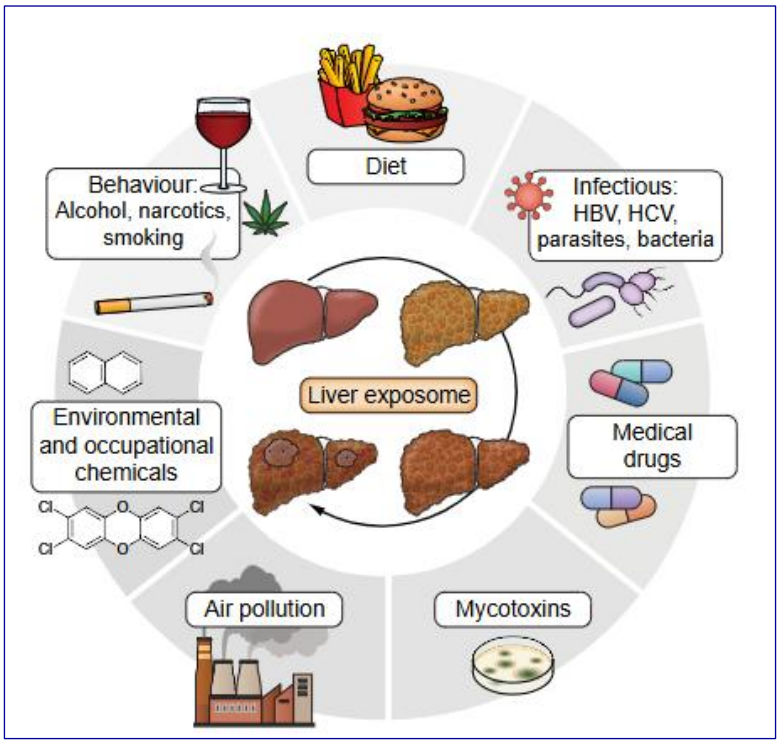


Fig 1: Determinants of the Liver Exposome and Their Role in Liver Disease Progression (Barouki et al., 2023)

Recent studies have highlighted a significant global rise in the prevalence of non-alcoholic fatty liver disease (NAFLD) and its progressive form, non-alcoholic steatohepatitis (NASH), with environmental toxins increasingly recognized as key contributing factors. According to a global epidemiological study, the estimated prevalence of NAFLD in 2016 was 41.12% among males and 37.32% among females, with the highest rates reported in Latin America (44.3%) and the Middle East and North Africa (36.5%) (Younossi et al., 2024). Similarly, the global prevalence of NASH was estimated at 15.79% in males and 16.48% in females, showing regional distributions closely paralleling those of NAFLD (Younossi et al., 2024). Environmental exposures play a significant role in disease progression. A meta-analysis conducted in 2025 demonstrated that exposure to ambient air pollutants such as PM 2.5, nitrogen oxides (NO2), and PM 10 significantly increases the risk of developing NAFLD and liver cirrhosis, with reported risk ratios of 1.33, 1.19, and 1.27, respectively (He et al., 2025). These findings support the hypothesis that environmental toxins contribute directly to hepatic inflammation and metabolic dysfunction. In the United States, future projections indicate a substantial increase in disease burden. A Markov model analysis predicts that the number of NAFLD cases will rise from 83.1 million in 2015 to 100.9 million by 2030, representing a 21% increase. Meanwhile, NASH cases are expected to increase by 63%, from 16.5 million to 27 million, with overall adult NAFLD prevalence projected to reach 33.5% by 2030 (Younossi et al., 2024). On a global scale, similar upward trends are expected. A recent analysis using Global Burden of Disease (GBD) data estimated a 94.49% increase in NAFLD incidence, rising from 24.86 million cases in 1990 to 48.35 million in 2021, with further growth projected to reach 78.6 million cases by 2050 (Le et al., 2025). This increase is attributed to factors such as aging populations, sedentary lifestyles, poor diet, and increasing environmental exposure. Ultimately, the convergence of obesity, environmental pollutants, and population aging is driving the rising global burden of NAFLD and NASH. These findings highlight the urgent need for integrated public health strategies that address both metabolic and environmental risk factors to mitigate disease progression and improve liver health outcomes worldwide (Prazeres, 2025).

Toxicant Accumulation, Detoxification Strategies in Hepato-Splenic Disorders

Chronic exposure to low-grade toxins can gradually disrupt vital physiological processes and weaken the immune system, ultimately contribute to the pathogenesis of a wide range of diseases, including degenerative and autoimmune conditions, as well as immune system dysfunctions that may increase susceptibility to infections. In Ayurveda, this condition is described as Dushi Visha—a form of residual, slow-acting toxin that accumulates in the body over time. Unlike acute poisons, Dushi Visha

remains latent within the system, often encapsulated by the Kapha dosha (a functional principle in Ayurveda associated with stability and fluid balance), allowing it to persist unnoticed for years. These toxins may originate from environmental pollutants, contaminated food, chemical substances, or biological sources, and remain in the body due to incomplete elimination or ineffective detoxification mechanisms. Over time, they are thought to undergo further degeneration, becoming more harmful under the influence of external factors such as climate, seasonal variations, dietary habits, and lifestyle factors like daytime sleeping or physical inactivity. Eventually, Dushi Visha is believed to invade and impair various tissues (dhatus), contributing to the onset of chronic, degenerative, or autoimmune conditions. This Ayurvedic concept underscores the importance of regular detoxification and lifestyle regulation to prevent the long-term accumulation of such subclinical toxins (Kishor et al., 2016). Wilson's disease, a genetic disorder characterized by excess copper accumulation, primarily in the liver and brain. Several studies have explored the relationship between serum ceruloplasmin levels and specific clinical subtypes of the disease. For instance, Cheng et al. (2017) found that elevated ceruloplasmin levels were more commonly associated with the hepatic (liver) subtype of Wilson's disease, whereas lower ceruloplasmin levels were often observed in individuals with the neurological subtype. These findings suggest that ceruloplasmin levels may serve as a valuable biomarker to help distinguish between the dominant clinical presentations of the disease. Given the role of copper accumulation in disease progression, managing copper levels becomes crucial for preventing organ damage, particularly in the liver and brain. A key factor in Wilson's disease pathogenesis is the disruption of copper homeostasis, which can exacerbate the generation of reactive oxygen species (ROS). One pathway that facilitates this is the Fenton reaction, a redox process wherein ferrous iron (Fe^{2+}) reacts with hydrogen peroxide (H_2O_2) to generate hydroxyl radicals (•OH). These highly reactive radicals can damage cellular components such as DNA, proteins, and lipids, contributing to oxidative stress, inflammation, and cell death. While lead (Pb) and cadmium (Cd) do not directly participate in the Fenton reaction, they disrupt metal homeostasis and antioxidant defence mechanisms, thereby amplifying Fenton-like reactions. This amplification results in an increased production of ROS, leading to widespread cellular damage. When lead and cadmium are present together, their combined toxicity significantly amplifies oxidative stress through several mechanisms. These include the inhibition of key antioxidant enzymes, such as glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT), which are essential for neutralizing ROS. Additionally, both metals deplete glutathione (GSH), a crucial intracellular antioxidant, and mobilize free iron or copper, further enhancing the generation of ROS via Fenton-like reactions. As a result, the toxicity induced by the combined presence of lead and cadmium is more severe than the effects of either metal alone, leading to substantial tissue damage.

In the kidneys, lead and cadmium induce nephrotoxicity by accumulating in the proximal tubules, where they trigger oxidative damage and suppress antioxidant defences. This results in tubular necrosis and contributes to the development of chronic kidney disease. In the liver, which plays a central role in detoxification and metal metabolism, lead and cadmium disrupt mitochondrial function, impair detoxification pathways, and inhibit antioxidant enzymes, causing mitochondrial dysfunction and lipid peroxidation, leading to hepatocyte death. In the blood, lead interferes with heme synthesis, while cadmium disrupts iron metabolism and induces haemolysis. These processes result in anaemia, characterized by impaired red blood cell function and decreased oxygen-carrying capacity. To counteract the toxic effects of lead and cadmium, certain essential minerals such as zinc, selenium, calcium, and iron exhibit antagonistic properties. These minerals help mitigate heavy metal-induced damage through several mechanisms. They compete with lead and cadmium for absorption and binding sites, reducing the bioavailability and accumulation of these toxic metals. Furthermore, these minerals stabilize enzymes and cellular structures, thus protecting against metal-induced disruption. Importantly, some minerals, like selenium, act as cofactors for antioxidant enzymes (e.g., glutathione peroxidase (GPx), which are crucial for detoxifying hydrogen peroxide and maintaining cellular redox balance. By supporting the body's antioxidant defence systems, these essential minerals can help reduce oxidative stress and mitigate cellular damage associated with heavy metal exposure. The pathway to organ damage from lead and cadmium exposure primarily involves oxidative stress and impaired metal homeostasis. In the liver, these metals disrupt mitochondrial function and antioxidant defence systems, leading to increased ROS production, lipid peroxidation, and hepatocyte injury. In the kidneys, lead and cadmium accumulate in the proximal tubules, where they induce oxidative damage, leading to tubular necrosis and the

development of chronic kidney disease. In some cases, this damage may also result in a Fanconi-like syndrome, characterized by impaired reabsorption of essential solutes. In the blood, the combined effects of lead and cadmium on heme synthesis and iron metabolism contribute to anaemia and reduced oxygen-carrying capacity (Matović et al., 2015; Hyder et al., 2013; Andjelkovic et al., 2019 and Niture et al., 2021). The liver plays a central role in processing and removing copper from the body, supporting its detoxification functions is crucial when treating copper build-up in conditions such as Wilson's disease. Medical treatments, dietary management, and liver-supportive supplements could play a crucial role in reducing copper accumulation and preventing further damage, particularly in individuals with the hepatic subtype of Wilson's disease, where copper build-up in the liver is most pronounced. From a modern toxicological perspective, environmental and industrial exposures to compounds such as ammonia, formaldehyde, lead, cadmium, and polychlorinated biphenyls (PCBs) can lead to their bioaccumulation in specific tissues. Lead is predominantly stored in the bone, cadmium in the liver and kidneys, and PCBs in adipose tissue. Additionally, inorganic particles like asbestos fibers can remain indefinitely in the body due to their poor biodegradability (Australia, 2012). Exposure to toxicants can lead to genomic alterations in key cancer driver genes within hepatocytes, initiating early molecular changes that precede malignant transformation, while also influencing the risk and severity of chronic liver diseases and hepatocellular carcinoma (HCC) (Barouki et al., 2023).

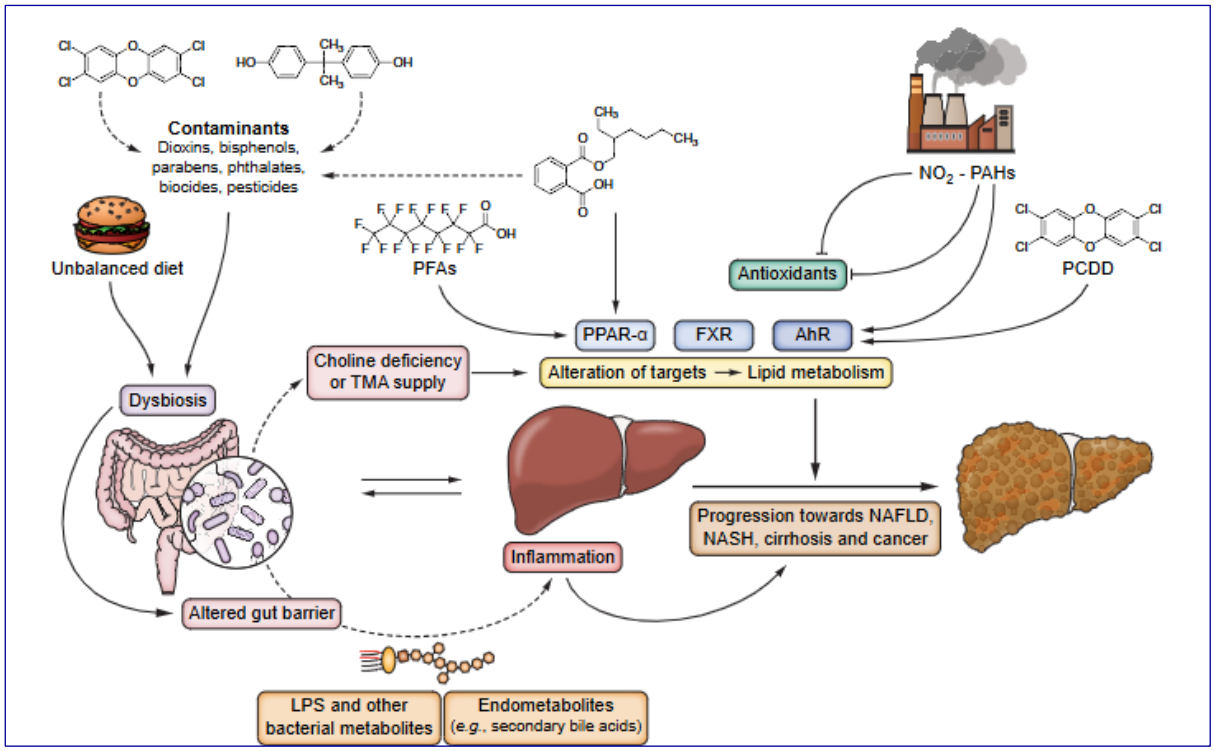


Fig 2: Impact of Food Contaminants and Environmental Pollutants on the Gut–Liver Axis and Liver Disease Development (Barouki et al., 2023)

Hence, it is essential to take up preventive measures and integrating evidence-based nutraceutical and phytotherapeutic interventions may help to enhance liver and spleen function, and support systemic detoxification pathways. This research article focuses on mechanistic investigations and clinical trials aimed at further validating the efficacy and safety of a formulation composed of *Mentha piperita* (peppermint), *Inula racemosa* extract (Indian elecampane), *Silybum marianum* (milk thistle), *Zingiber officinale* (ginger), *Bacillus coagulans* (probiotic), *Beta vulgaris* (beetroot), and *Andrographis paniculata* in the management of toxin-induced organ dysfunction.

Mentha piperita, commonly known as peppermint, is widely recognized for its diverse pharmacological properties, including antioxidant and antiperoxidative effects, attributed to bioactive constituents such as eugenol, caffeic acid, rosmarinic acid, and α-tocopherol. Additionally, it exhibits antifungal, antibacterial, antimutagenic, chemopreventive, and radioprotective activities. Mentha has also been identified as a hematopoietic stimulant and offers protective effects against

gastrointestinal tract damage. A study conducted by Sharma et al. (2007) investigated the protective role of *Mentha piperita* in arsenic-induced hepatotoxicity using albino mice. The research identified key bioactive compounds in the plant, including a rich composition of polyphenols such as rosmarinic acid, eriocitrin, cinnamic acid, and caffeic acid, as well as flavonoid glycosides like narirutin, luteolin-7-O-rutinoside, isorhoifolin, and hesperidin. It also contains significant amounts of terpenes and related phytochemicals such as limonene, cineole, menthone, menthofuran, isomenthone, carvone, pulegone, and menthyl acetate (Chakraborty et al., 2022). Among these, eugenol, a naturally occurring allylbenzene found in *M. piperita* leaves has drawn particular interest for its ability to induce detoxification enzymes involved in conjugating xenobiotics. Moreover, eugenol is known for its potent antioxidant and hepatoprotective properties. In Sharma et al.'s study, Mentha extract significantly influenced key biochemical markers associated with liver function and oxidative damage, including alkaline phosphatase (ALP), lactate dehydrogenase (LDH), reduced glutathione (GSH), acid phosphatase (ACP), serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), and lipid peroxidation (LPO) highlighting its therapeutic potential in hepatoprotection. In a related study, Samarth et al. (2006) evaluated the chemopreventive, antigenotoxic, and antioxidative efficacy of Mentha piperita in a medium-term murine model of benzo[a]pyrene (BaP)-induced lung carcinogenesis. BaP, classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC), serves as a model genotoxicant commonly encountered through cigarette smoke, grilled foods, and polluted environments. Upon metabolic activation, BaP generates reactive intermediates such as benzo[a]pyrene diol epoxide (BPDE), which form DNA adducts that result in mutations, chromosomal aberrations, and micronuclei formation—assessed via micronucleus and chromosomal aberration assays. Furthermore, BaP enhances oxidative stress through the generation of reactive oxygen species (ROS), leading to lipid peroxidation, protein oxidation, and depletion of endogenous antioxidants including superoxide dismutase (SOD), catalase (CAT), and GSH, along with elevated malondialdehyde (MDA) levels, typically measured using biochemical assays such as ELISA. Remarkably, treatment with Mentha piperita led to a 61.26% reduction in lung tumor incidence, a marked decrease in chromosomal aberrations and micronuclei frequency in bone marrow cells, and a restoration of hepatic and pulmonary antioxidant enzyme activity, demonstrating its strong chemopreventive and antioxidant potential (Samarth et al., 2006; Bukowska et al., 2022).

Inula racemosa, known as *Pushkarmula/ Puskara* in Ayurveda, is a well-documented medicinal herb traditionally used for its detoxifying, cardioprotective, and respiratory-supportive properties. It is classified as possessing Tikta (bitter) and Kaṭu (pungent) Rasa (taste), Uṣṇa Virya (heating potency), and Kaṭu Vipaka (pungent post-digestive effect), making it effective in the elimination of Ama (incompletely digested food particle) and in the regulation of Vata doshas (*bio-energy governing movement, composed of air and ether; associated with nervous system activity and bodily motion*) and Kapha doshas (bio-energy governing structure and stability, composed of water and earth; associated with immunity, lubrication, and cohesion in the body). Pharmacologically, *Inula racemosa* has demonstrated expectorant, bronchodilator, anti-inflammatory, and digestive stimulant effects. It is frequently employed in Ayurvedic formulations such as *Rasnadi Kvatha Curṇa*, where it aids in the detoxification of the musculoskeletal and respiratory systems. Additionally, it may be included in certain variants of *Dasamularişţa* to support systemic detox and respiratory health. These applications underscore its relevance in both classical detox protocols and contemporary integrative medicine (API Vol 4). The root extract of *Inula racemosa* has garnered attention for its potent antioxidant properties, primarily attributed to its high content of sesquiterpene lactones such as alantolactone and isoalantolactone, which are known to modulate redox signaling pathways. These compounds facilitate the activation of the nuclear factor erythroid 2-related factor 2 (Nrf2), a key transcription factor involved in the cellular antioxidant response. Upon activation, Nrf2 translocates to the nucleus and binds to the antioxidant response element (ARE), initiating the transcription of various cytoprotective genes including heme oxygenase-1 (HO-1) and NAD(P)H quinone dehydrogenase 1 (NQO1), thereby enhancing cellular defense mechanisms against oxidative stress. Natural plant-derived extracts are increasingly explored for their potential in cancer therapy due to their biocompatibility and selective cytotoxic effects. Preliminary evidence suggests that aqueous extracts can exhibit differential activity, showing minimal toxicity to normal cells while impairing the viability of cancer cells. For instance, aqueous extracts have been observed to remain non-toxic to normal kidney epithelial (NKE) cells up to concentrations of 600 mg/ml, while inducing dose-

dependent morphological alterations in renal carcinoma cell lines such as A498 and ACHN at concentrations above 400 mg/ml and 200 mg/ml, respectively. This selective cytotoxicity highlights the potential of aqueous plant extracts as promising candidates for adjunct or alternative cancer therapies (Chaturvedi, 2011; Mohan & Gupta, 2019). Experimental studies have demonstrated that administration of *Inula racemosa* root extract significantly increases the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx), and restores reduced glutathione (GSH) levels, resulting in improved redox balance and reduced lipid peroxidation in oxidative stress-induced models (Liu et al., 2022). In addition, it is essential to know that as a master transcription factor, Nrf2 orchestrates the expression of antioxidant and protective genes, facilitating the skin's adaptive response to environmental challenges like UV radiation and contributing to the maintenance of skin integrity (Chaiprasongsuk & Panich, 2022). These findings suggest that the bioactive constituents of *Inula racemosa* root act through the Nrf2-ARE signaling axis to re-establish redox homeostasis, highlighting its therapeutic potential in managing oxidative stress-related conditions (Mohan & Gupta, 2019).

The hepatoprotective potential of *Silybum marianum* (milk thistle) has been acknowledged for over two thousand years for its traditional use. Its medicinal value is attributed to a complex of bioactive flavonolignans, including silybin (silibinin A and B), silychristin, silydianin, isosilybin, dehydrosilybin, as well as additional polyphenolic compounds such as apigenin, deoxysilychristin, and deoxysilydianin (Murphy et al., 2000; Wang et al., 2020). These constituents collectively form silymarin, a standardized extract known for its liver-protective effects. Silymarin confers hepatoprotection through several interrelated mechanisms. It stabilizes hepatocyte membranes, preventing the entry of hepatotoxins, and acts as a potent antioxidant by scavenging free radicals and inhibiting lipid peroxidation. It has shown protective effects in experimental models of liver injury induced by a range of toxins, including carbon tetrachloride, paracetamol, halothane, alloxan, and microcystin. Furthermore, it modulates the cytochrome P450 enzyme system, reducing the metabolic activation of hepatotoxins such as those from *Amanita phalloides.* Silymarin also stimulates hepatic protein synthesis and ribosomal RNA production, promoting liver tissue regeneration primarily in damaged livers (Corchete, 2008). In addition to its cellular protective actions, silymarin exhibits anti-inflammatory and antifibrotic effects, while clinical evidence suggests its administration may lead to reduced serum liver enzymes (ALT, AST, GGT), improved lipid profiles characterized by decreased total cholesterol and increased high-density lipoprotein (HDL) and improved outcomes in various liver disorders. These multifunctional properties support its therapeutic potential in the management of hepatic diseases of diverse etiologies, including those of toxic, viral, or alcoholic origin (Bahmani et al., 2015).

Zingiber officinale, commonly known as ginger, is a perennial rhizomatous herb from the family Zingiberaceae, widely cultivated across South and Southeast Asia in both humid lowlands and high-altitude regions. It has been used since at least the fourth millennium B.C. for its culinary and medicinal properties, making it one of the most ancient herbal remedies known to humankind. Traditionally, ginger is recognized as a potent nutraceutical, particularly for its diverse actions on the gastrointestinal system, including the management of constipation, indigestion, nausea, and vomiting. It also serves as a stimulant and carminative agent. In traditional Chinese and Ayurvedic medicine, the dried rhizome of *Zingiber officinale* is widely utilized for its pharmacological effects. In traditional contexts, *Zingiber officinale* Rhizoma (ZOR) is employed to release the exterior and dispel cold, arrest nausea and vomiting, resolve phlegm, relieve cough, and manage functional dyspepsia, epigastric discomfort, and food poisoning particularly from fish and shellfish. It is also valued for its anti-ulcerative and anti-emetic properties (Semwal et al., 2015; Kaur et al., 2015; Ma et al., 2020). Modern pharmacological research has substantiated many of these traditional uses and has further identified a broad spectrum of bioactivities, including prokinetic and digestive effects, enhanced peripheral circulation, blood lipid and glucose regulation, and mitigation of vestibular disorders. ZOR also exhibits significant inhibitory effects against Helicobacter pylori, particularly CagA-positive strains, largely attributed to its antioxidant mechanisms, such as free radical scavenging and inhibition of lipid peroxidation (Kaur et al., 2015). The biological activity of ginger is primarily attributed to its phytochemical constituents: gingerols, shogaols, paradols, and zingerone. Among these, [6]-gingerol is the most abundant in fresh ginger and is responsible for its pungency and a wide range of therapeutic effects. Both 6-gingerol and 10-

gingerol have demonstrated anti-cancer activity, notably in breast cancer cells, by modulating components of the MAPK signalling pathway such as p38 and ERK, resulting in cell cycle arrest and/or apoptosis. Upon drying, gingerols convert to shogaols, which have heightened pungency and increased bioactivity. Thermal processing further transforms gingerols into zingerone, a milder compound with potent antioxidant and anti-inflammatory properties (Kaur et al., 2015; Spence, 2023). These compounds also interact with the Transient Receptor Potential Vanilloid 1 (TRPV1) receptor a non-selective cation channel involved in the sensory perception of heat, pain, and inflammation. Activation of TRPV1 by ginger constituents contributes not only to ginger's characteristic pungency but also to its therapeutic actions in reducing pain and inflammation (Semwal et al., 2015; Spence, 2023). Gingerols, the primary bioactive constituents of ginger, have also been shown to exert multifaceted effects on digestive enzyme secretion and activity. These compounds stimulate the secretion of pancreatic enzymes such as lipase, amylase, trypsin, and chymotrypsin, potentially through modulation of cholinergic pathways that enhance acetylcholine-mediated exocrine output. Additionally, gingerols may influence gastrointestinal hormone levels, including gastrin and secretin, which further regulate enzyme secretion. Beyond pancreatic stimulation, gingerols have been reported to upregulate the activity of brush-border membrane enzymes such as sucrase, maltase, leucine aminopeptidase, glycyl-glycine dipeptidase, and γ-glutamyl transpeptidase in the jejunal mucosa. These effects are likely facilitated by the antioxidant and anti-inflammatory properties of ginger, which help maintain the integrity and functionality of intestinal epithelial cells. Furthermore, gingerols may enhance digestive efficiency by improving gut motility and mesenteric blood flow, thereby optimizing the interaction between digestive enzymes and their substrates. Collectively, these mechanisms underscore the role of ginger in promoting gastrointestinal function and nutrient assimilation (Platel & Srinivasan, 1996; Kaur et al., 2015). A randomized controlled trial on mice divided into four groups demonstrated that ginger may serve as both a preventive and anti-hepatotoxic agent. In addition to causing liver damage, lead acetate exposure in Group B mice resulted in significant haematological alterations, including decreased haemoglobin (Hb) concentration, packed cell volume (PCV), and red blood cell (RBC) count—indicators of anaemia and bone marrow suppression. A marked increase in white blood cell (WBC) count was also observed, indicating an inflammatory response. In contrast, Group D mice, which received co-treatment with ginger extract, showed substantial improvement in haematological parameters, with values approaching normal levels (Imafidon & Abba, 2024). These findings suggest that ginger extract provides protective effects on the hematopoietic system, likely due to its antioxidant properties, free radical scavenging activity, and potential to stimulate erythropoiesis. This underscores ginger's broader systemic protective role against lead-induced toxicity, extending beyond liver protection to include restoration of haematological integrity. In Ayurveda, dry ginger (Suṇṭhi) is central to numerous classical formulations for gastrointestinal and postpartum health. Saubhagyasunṭhi is a postnatal formulation that supports digestion and maternal recovery. Trikatu Curṇa ("Powder of the Three Pungents") combines ginger with black pepper (Marica) and long pepper (Pippali) to stimulate digestive fire (Agni), reduce bloating, and enhance nutrient absorption. Similarly, Saubhagya Vaṭi is used postpartum to restore gastrointestinal balance and promote tissue healing. Vaisvaanara Curṇa, named after the Vedic concept of universal digestive energy, is indicated for regulating bowel function, relieving gas, and treating chronic digestive disturbances. Ginger is further recommended in classical Ayurvedic texts for the treatment of conditions such as Agnimandya (sluggish digestion), Adhmana (abdominal bloating), Paṇḍu (anemia), Udara Roga (abdominal diseases), and Amavata (a Vata-related joint disorder resembling rheumatoid arthritis) (API Vol. 1).

Bacillus coagulans (Currently *Weizmannia coagulans*) is a Gram-positive, spore-forming, lactic acid-producing probiotic bacterium known for its remarkable resistance to heat, acidity, and desiccation. These characteristics make it particularly suitable for use in nutraceutical formulations, where it plays a crucial role in supporting gastrointestinal health and maintaining a balanced gut microbiota essentially by altering the phylogenetic relationships and abundance of microbial taxa (Hong et al., 2005; Wu et al., 2024). The *B. coagulans* strain BDU3 has demonstrated inhibitory activity against various food-borne pathogens, including *Bacillus cereus*, *Staphylococcus aureus*, *Enterococcus* spp., *Lactobacillus* spp., and *Micrococcus luteus*. Additionally, it exhibits antifungal properties against fungal species such as *Botrytis cinerea*, *Fusarium pallidoroseum*, and *Fusarium moniliforme*. *W. coagulans* is also recognized for its potential in alleviating or preventing antibiotic-associated Diarrhea (AAD) and irritable bowel syndrome (IBS),

particularly in pediatric populations. A study by Aida et al. reported that supplementation with *Bacillus coagulans* in broiler chickens enriched the expression of inflammatory response genes associated with Th1 cells and M1 macrophages, including the upregulation of IL8L2 and SOCS3. Additionally, W. coagulans modulated immune-regulatory genes such as CCL17 and CCL18, contributing to a more balanced immune response. These immunological changes were accompanied by significant shifts in the gut microbiota, marked by an increased abundance of beneficial genera such as *Alistipes*, *Blautia*, and *Bifidobacterium*, and a reduced presence of potentially pathogenic genera including *Escherichia-Shigella* and *Desulfovibrio*. Such microbial alterations are associated with enhanced gut barrier integrity and increased production of short-chain fatty acids (SCFAs), particularly butyrate, which collectively contribute to improved gut health. Furthermore, the study employed Gene Ontology (GO) enrichment analysis to compare chicken genes with their human homologs, offering valuable cross-species insights (Aida et al., 2023). Overall, *B. coagulans* supplementation appears to support gut immunity, enhance resilience to infection, and maintain immune homeostasis under stress. Moreover, the bacterium is a notable producer of the enzyme lipase, which has been investigated for applications across multiple industries, including pharmaceuticals, industrial biotechnology, food technology, and environmental management (Konuray & Erginkaya, 2018). Given its broad spectrum of health benefits, especially in promoting Gastrointestinal Tract (GIT) health and supporting Probiosis, *B. coagulans* is increasingly incorporated into health supplements, often in combination with Ayurvedic herbs and bioactive compounds.

Beta vulgaris (beetroot) is a widely consumed functional food in Europe and Asia, valued for its high nutritional content and rich composition of bioactive compounds, including phenolic acids, flavonoids, and betalains. The two main components of Beetroot are betaine and betalain. Its extract has demonstrated antioxidant, anti-inflammatory, antibacterial, hepatoprotective and antihypertensive properties, supporting its potential use as a dietary health supplement (Bashir et al., 2024). In a case controlled prospective study, Betaine, an osmolyte and methyl donor derived from beetroot, participates in hepatic transmethylation reactions, particularly in the remethylation of homocysteine to methionine. Through its role in one-carbon metabolism, betaine contributes to the regulation of lipid homeostasis and attenuates hepatic triglyceride accumulation, thereby exerting a hepatoprotective effect and potentially mitigating the progression of non-alcoholic fatty liver disease (NAFLD) (Srivastava et al., 2019). Another study reported that betanin exhibits high antiradical activity at pH values above 4. This enhanced activity is further attributed to strong electronic conjugation between the betalamic acid and cyclo-DOPA-5-O-β-D-glucoside moieties, which contributes significantly to its antioxidant potential (Gliszczyńska-Świgło et al., 2006)

Andrographis paniculata, commonly known as the 'King of bitters' or 'Bhunimba' has been traditionally used in Ayurvedic medicine in India for its notable hepatoprotective properties (Bhaishajya Ratnavali Vol 5; Bardi et al., 2014; Deshpande & Gothalwal, 2015). The plant's therapeutic effects are primarily attributed to three major diterpene compounds: andrographolide, neoandrographolide, and 14-deoxyandrographolide (Chauhan et al., 2019). It is known for its Anti-diabetic, Anti-cancer, Anti-bacterial, Anti-inflammatory, hepatoprotective, Neuroprotective, immunostimulatory and immunomodulatory effects (Wongnawa et al., 2012; Akbar, 2017 and Saka et al., 2025). A controlled in vivo study was conducted using rats, which were randomly divided into four experimental groups. Group I served as the untreated normal control, comprising healthy rats with no exposure to ethanol or therapeutic agents. Group II received ethanol alone to induce hepatotoxicity, thereby modelling alcohol-induced liver injury. Group III was administered ethanol to initiate hepatic damage, followed by treatment with an aqueous extract of *Andrographis paniculata* to evaluate its potential hepatoprotective effects. Group IV was similarly subjected to ethanol-induced liver injury and subsequently treated with silymarin, a well-established hepatoprotective reference drug. Post-treatment analysis indicated that both *A. paniculata* and silymarin conferred protective effects against ethanol-induced liver damage. Notably, *A. paniculata* exhibited antioxidant properties, including free radical scavenging activity, which may contribute to its hepatoprotective action (Sivaraj et al., 2011).

The selected ingredients were chosen based on their complementary mechanisms of action and their potential to produce synergistic or additive therapeutic effects when combined. To assess the efficacy of the final encapsulated form of this proprietary nutraceutical dietary supplement, a clinical study was conducted involving human subjects diagnosed with *Yakrut Vikara* (liver

disorders), *Kaamala* (Jaundice), and *Pleeha Roga* (spleen disorders). Participants exhibited symptoms such as excessive fatigue, shortness of breath, loss of appetite, nausea, abdominal pain, general weakness, and abdominal bloating. This study was undertaken to validate the supplement's therapeutic potential and ensure its safety and effectiveness in improving the clinical outcomes of individuals suffering from these chronic conditions.

Materials and Methodology

Clinical Validation of a Nutraceutical Capsule Formulated with Ayurvedic Herbs

Study Design and Ethical Approval

This study was designed as a prospective, Phase I, open-label, single-centre, community-based pilot clinical trial to assess the efficacy of a nutraceutical capsule - Detoxy-One is formulated with a combination of Ayurvedic herbs. The trial was conducted under the supervision of the Contract Research Organization (CRO), Ashram Siddha Research Institute. The study protocol (Protocol Number: DT-95-04-24) was reviewed and approved by the Institutional Ethics Committee for Clinical Research of the CRO, which is constituted under Rule 7 and registered under Rule 8 of the Central Drugs Standard Control Organization (CDSCO), operating under the Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India. The study complied with the ethical guidelines for biomedical research on human participants as per the 2006 AYUSH-ICMR guidelines. Written informed consent was obtained from all participants prior to enrolment.

Study Population

The trial was conducted in Salem, Tamil Nadu, India, where the estimated prevalence of Yakrut Vjkaara (liver disorders), Kaamala (Jaundice), and Pleeha Roha (spleen-related disorders) exceeds 30% of the population. These conditions are often associated with symptoms such as excessive tiredness, shortness of breath, abdominal bloating, nausea, loss of appetite, and fatigue. A total of ten participants who presented with such symptoms were enrolled in the trial. The study was conducted over a period of 30 days, from April 8, 2024, to May 7, 2024.

Participants were selected following an open-label, non-randomized community-based recruitment process. Inclusion and exclusion criteria were determined through thorough clinical examination and history taking. Patients above the age of 65 years or with a history of osteoarthritis, drug or alcohol abuse, night or shift work, diabetic complications, psoriatic arthritis, or endocrine disorders were excluded. Additionally, participants were withdrawn from the study if their symptoms worsened or if they developed any serious condition requiring urgent medical attention.

Intervention

The investigational product administered in this study was a nutraceutical capsule containing a standardized blend of Ayurvedic and botanical ingredients. Each capsule was formulated with cold-compressed essential oil of *Mentha piperita* (peppermint), standardized for menthol content; root extract of *Inula racemosa* (Indian elecampane) containing approximately 13% saponins; seed extract of *Silybum marianum* (milk thistle) standardized to approximately 70% silymarin; and rhizome extract of *Zingiber officinale* (ginger) containing around 2% gingerols. The formulation also included *Bacillus coagulans*, a probiotic strain delivering approximately 15 billion spores per gram; *Beta vulgaris* (beetroot) root extract standardized to contain 0.3% betanin and approximately 5.2% nitrates; and leaf extract of *Andrographis paniculata* standardized to contain approximately 11% andrographolide. Participants were instructed to take one to two capsules orally, twice daily after meals, with lukewarm water, for the duration of the study. In addition to the capsule regimen, all participants received lifestyle counselling that included personalized dietary recommendations, physical activity guidance, and general health education to support therapeutic outcomes and encourage self-management of their condition. Compliance monitoring was conducted on patients to ensure adherence, participants were instructed to complete weekly adherence diaries to record daily intake.

Clinical Assessment and Evaluation

Comprehensive clinical evaluations were conducted on Day 1 (baseline) and Day 30 (end of study) by qualified Siddha and Ayurveda practitioners. Detailed case records were maintained for each participant throughout the study. Diagnostic assessments were carried out in accordance with traditional Siddha diagnostic protocols which involves the eightfold diagnostic method Envagai Thaervu, Tridosha Naadi a pulse diagnosis to assess the balance of Vata, Pitta, and Kapha, and Saptha Dhatu Thaervu meaning evaluation of the seven body tissues. These assessments provided a holistic understanding of the participants' health status and were used to monitor progress during the study. The primary outcome measure was defined as a minimum 10% reduction in presenting symptoms, as reported by the participants and confirmed by the

clinical judgment of the attending physicians. This reduction was considered a clinically significant indicator of therapeutic success. Participants received detailed information about the study, including potential side effects, expected benefits, the right to withdraw at any time, and procedures for follow-up and referral, all communicated in their native language to ensure complete understanding. This study cohort comprised 10 patients, including 6 males and 4 females as depicted in figure 3. Participants were divided into two age-based groups: the first group included individuals aged 22 to 44, and the second group included those aged 45 to 60 as depicted in figure 4. The efficacy of the nutraceutical supplement was evaluated over a one-month period by monitoring reductions in symptoms such as excessive tiredness, shortness of breath, abdominal bloating, nausea, loss of appetite, and fatigue.

Figure 3: Gender ratio of the Patients

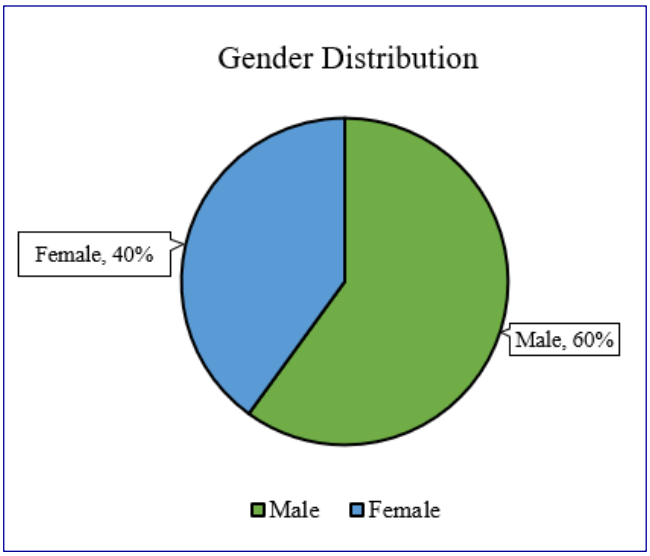
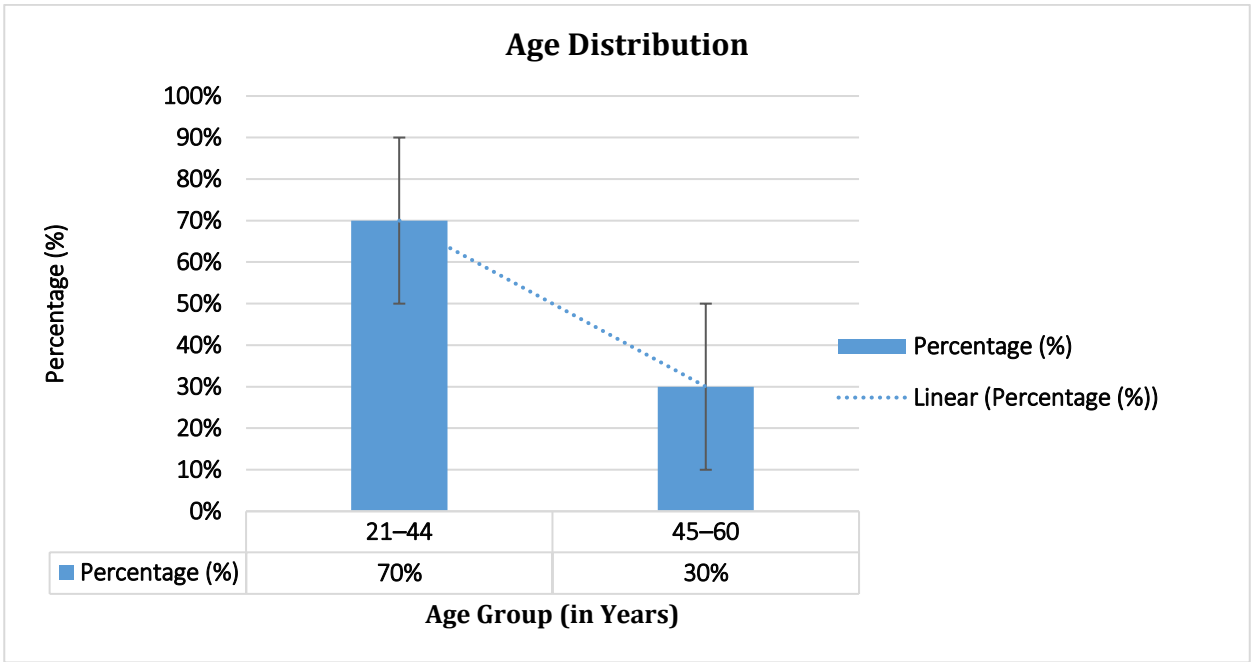


Figure 4: Categorization of Patients According to Age



Results

The clinical study results of the Phase I, single centre, Open labelled, human-pilot controlled study for the nutraceutical product formulated with the ayurvedic blend, as illustrated in the table 1 and figure 5, indicate a favourable therapeutic impact across various health parameters. The participant group consisted of 40% females and 60% males, with the majority falling within the 21–44 age range (70%), followed by 45–60 years (30%). Across symptom categories, there was a marked reduction in fatigue and shortness of breath, with participants reporting significantly lower severity scores after

intervention. Improvements were also observed in appetite and nausea, as most individuals transitioned from experiencing moderate or severe symptoms to reporting only mild or no discomfort. Similarly, abdominal pain and bloating saw notable alleviation, reflecting a clear downward trend in symptom intensity. These findings culminate in a strong overall clinical outcome, with over 80% of participants reporting substantial symptom relief and rating their health status as either "Improved" or "Significantly Improved" by the end of the study. This underscores the potential efficacy of the encapsulated nutraceutical product in managing both gastrointestinal and systemic symptoms.

The overall clinical outcome, as illustrated by the treatment response data, demonstrated a high level of therapeutic efficacy. A significant majority of patients (80%) exhibited very good improvement, characterized by the resolution of all four assessed symptoms. An additional 10% of patients showed moderate improvement, with relief in 2 to 3 symptoms, while the remaining 10% experienced only mild improvement, with less than two symptoms resolving. These findings suggest that the intervention was highly effective for most individuals, with a relatively small proportion requiring further clinical attention or alternative management strategies. Figure 6 provides a comprehensive depiction of the intervention's impact on patients presenting with symptoms including excessive tiredness, shortness of breath, abdominal bloating, nausea, loss of appetite, and fatigue, thereby offering valuable insight into the clinical effectiveness of the intervention across this symptomatic profile.

Table 1: Descriptive Statistics of Symptom Improvement Over Time (or) Symptom Improvement Distribution Across Age Groups

Age Group (in Years)	Fatigue and Shortness of Breath			Loss of Appetite and Nausea			Abdominal Pain and Bloating		
	Improvement		% Improvement	Improvement			Improvement		% Improvement
	15 Days	30 Days		15 Days	30 Days		15 Days	30 Days	
21–44	6	6	100%	4	3	75%	4	3	75%
45–60	4	3	75%	6	5	83%	6	5	84%

Figure 5: Symptom Improvement Over Time Stratified by Age Group During Supplement Use

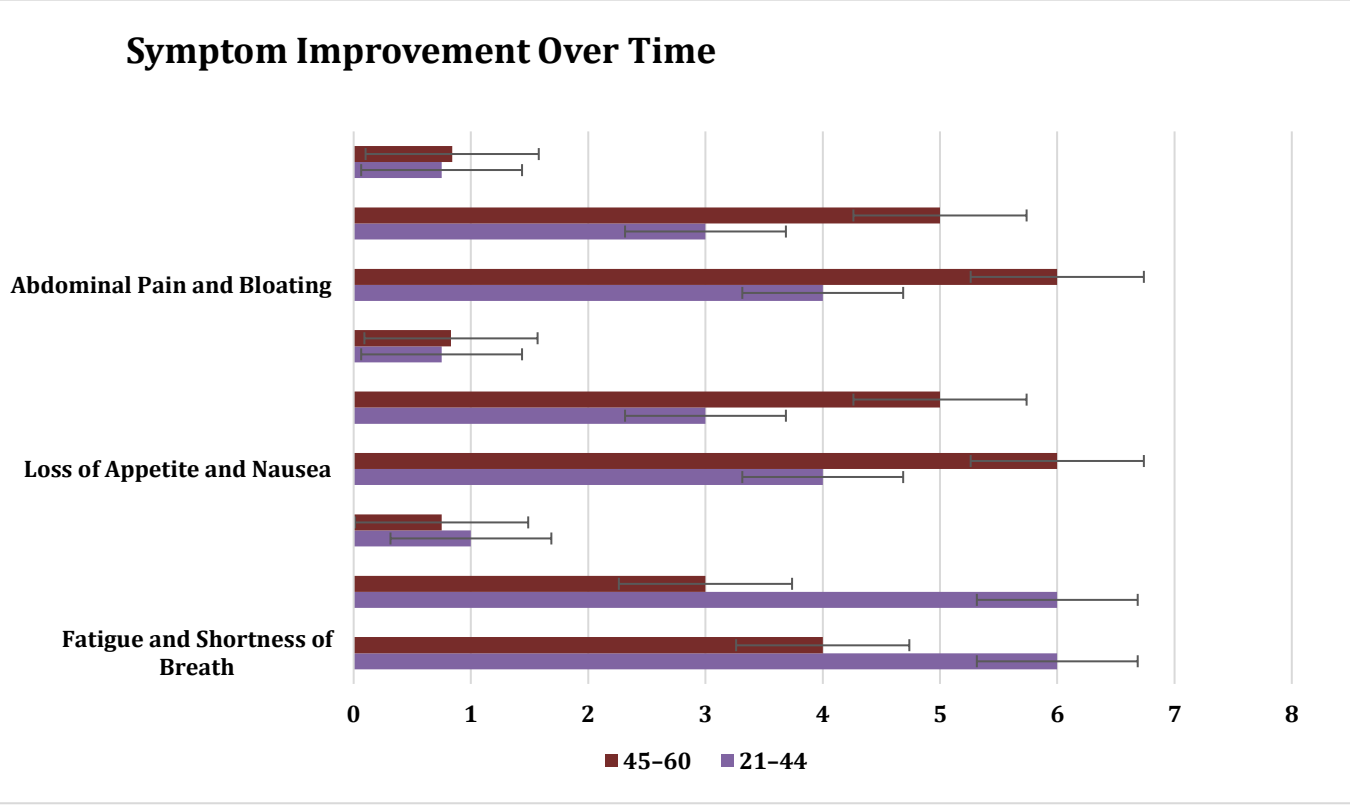
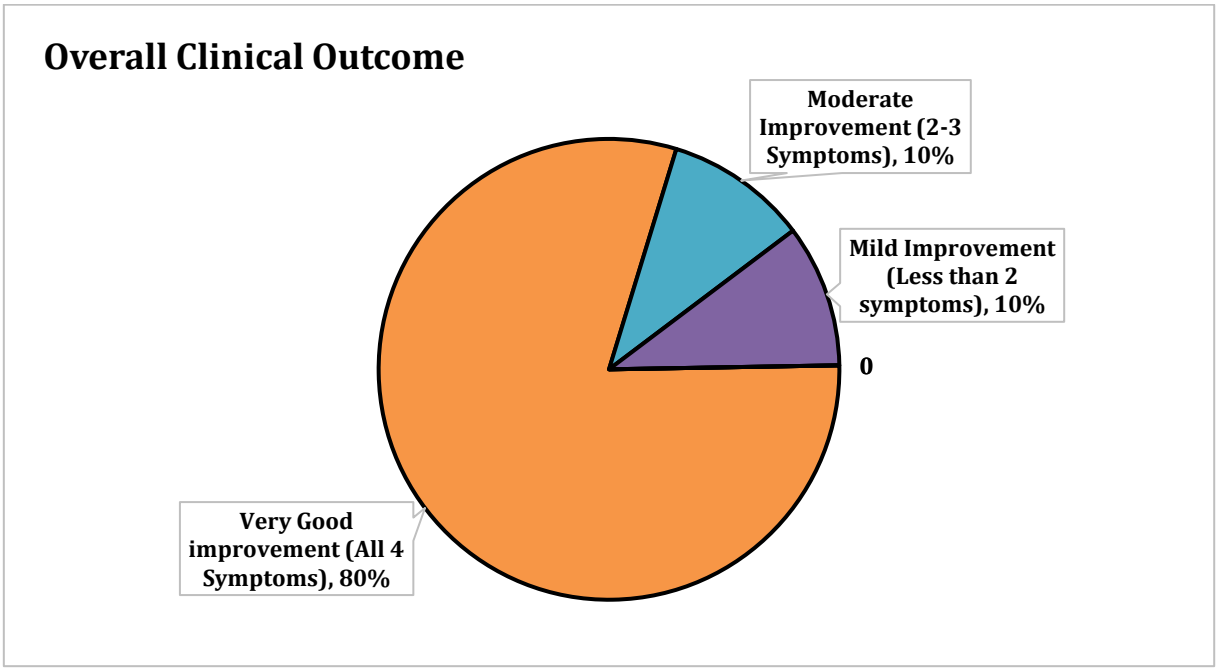


Figure 6: Overall Reduction in Clinical Symptoms Among Treated Patients (N = 10) (or) Effect of Intervention on Clinical Symptom Reduction in Study Cohort (N = 10)



DISCUSSION

In recent decades, rapid lifestyle changes and increased technological dependency have contributed to a rising global burden of chronic and lifestyle-related diseases. In parallel, there has been growing interest in traditional systems of medicine, particularly Ayurveda, due to their emphasis on holistic, alleviating the root-cause–oriented approaches and their generally favourable safety profiles. As a result, there is an increased consumer demand for natural, plant-based formulations that offer therapeutic or preventive benefits without the adverse effects commonly associated with certain modern pharmaceuticals. Nutraceutical products formulated with 100% natural ingredients have gained popularity as adjunctive or preventive health supplements, aimed at improving health outcomes, supporting physiological functions, and reducing disease risk in a non-toxic manner (Krishna et al., 2020; Tovoli et al., 2024). This research focuses on the accumulation of toxic substances arising from both environmental exposures and endogenous metabolic processes. Environmental sources include emissions from industrial activities and the presence of pollutants in air, water, or soil, which can lead to bioaccumulation over time. Additionally, metabolic toxicity may result from the chronic intake of substances such as alcohol or other low-dose xenobiotics that, although individually insignificant, can cumulatively exert harmful effects. These toxicants may progressively impair vital organs, particularly the liver and spleen, due to their central roles in detoxification and immune function. The findings highlight the potential for such cumulative exposure to trigger a cascade of adverse physiological outcomes, reinforcing the need for early detection and preventive strategies in both environmental health and clinical toxicology (Wahlang et al., 2019).

Given the persistence and systemic toxicity of these substances, preventive healthcare strategies are of critical importance. Moreover, therapeutic interventions aimed at supporting detoxification and the elimination of accumulated toxins are essential for maintaining systemic homeostasis. In this context, nutraceuticals—bioactive compounds derived from food sources as well as Ayurvedic medicinal herbs and formulations, offer promising avenues for both preventive and adjunctive treatment. Traditional Ayurvedic texts describe various herbal remedies with detoxifying and hepatoprotective properties. Modern scientific validation of these remedies highlights their potential in mitigating the clinical manifestations of Yakṛt Vikāra (liver disorders), Kāmala (hepatitis), and Plīha Roga (spleen disorders). Patients suffering from these conditions often present with fatigue, anorexia, nausea, abdominal pain, bloating, and dyspnoea, which can significantly impair quality of life. The formulation used in this study contains several ingredients *Mentha piperita* (peppermint), *Inula racemosa* extract (Indian elecampane), *Silybum marianum* (milk thistle), *Zingiber officinale* (ginger), *Bacillus coagulans* (probiotic), *Beta vulgaris* (beetroot), and *Andrographis paniculata* with individually documented bioactivity relevant to liver health and detoxification. While direct clinical comparisons are

limited, these components have shown promise in supporting hepatocellular function, reducing oxidative stress, and improving gut-liver axis dynamics.

In the trial, patients receiving the encapsulated formulation demonstrated at least an 80% clinical improvement across several outcome measures. Although the product has been commercially available and widely used without significant reported adverse effects, the lack of prior peer-reviewed clinical data necessitated this study. This study fills that gap by providing preliminary evidence supporting both the safety and efficacy of the formulation. Notably, we observed significant reductions in symptoms such as fatigue, loss of appetite, nausea, abdominal discomfort, and skin pigmentation anomalies, suggesting improved detoxification of the body. However, this investigation was limited by its single-centre design, small sample size, and relatively short duration of approximately one month. Despite these limitations, the findings provide valuable preliminary insights. To confirm and generalize these outcomes across broader populations, further validation through multicentre, long-term studies is necessary. Notably, over the past decade, multiple consumers have not reported any adverse or negative effects.

CONCLUSION

The formulation of the nutraceutical product using Ayurvedic herbs has demonstrated promising outcomes in a Phase I, single-centre clinical trial, with approximately 80% improvement reported and no adverse effects observed. These findings suggest that herbal supplements may contribute to maintaining overall physiological balance, particularly when compared to certain modern pharmacological interventions. As the nutraceutical industry continues to expand, there is an increasing emphasis on scientific validation of product efficacy through clinical or preclinical studies. In this context, network pharmacology has emerged as a valuable tool for cost-effective screening and mechanistic insights prior to human trials. Despite the commercialization of such products, it is crucial that the use of nutraceuticals especially those claiming therapeutic benefits be supervised by qualified healthcare professionals to ensure appropriate usage and to prevent potential contraindications. Continued research and standardized clinical protocols are essential for integrating these products safely and effectively into mainstream health management.

Participant protections and ethics

To protect human participants, the protocol was written according to general ethical guidelines, such as the Declaration of Helsinki and Good Clinical Practice, approved by the institutional ethical committee of the organization. The study participant consent process includes information about potential risks, benefits, alternatives, and responsibilities during the trial. Before participants agree to participate in this trial, researchers will explain this information in detail in person.

Data and safety monitoring

Regular monitoring, as outlined in a standard operating procedure, will be performed to ensure high data quality. Monitors from IEC will assess whether the case report forms are completed accurately and if the recruiting and treatment procedures are executed correctly according to the protocol. Investigators will be contacted to discuss the need for revising the study protocol, inclusion criteria, and other critical issues. Both investigators and independent researchers will evaluate the clinical trial's progress, review any severe adverse events, and determine whether these events are acceptable or if modifications to the trial or a cessation is necessary. Case Sheets are prepared for each patient, and all records and vouchers will be kept at the treatment centre for three years.

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