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Effect of Snehpana (Lipid Based Drug Delivery System) with Shatpala Ghrit in Non-Alcholic Fatty Liver Diseases

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Abstract

Among all the Drug Delivery Systems, Snehpana (~Lipid Based Drug Delivery System) is being widely used because this facilitates uniform distribution and absorption of fat and water-soluble chemical constituents. Due to their effective size-dependent properties and challenges related to the solubility and bioavailability of water-soluble drugs, this system holds a significant advantage. Numerous studies have highlighted the potential of lipid-based formulations in managing chronic and life-threatening diseases. Shatpala ghrit (SG) shows promise for use in clinical applications. Previously no clinical and animal studies data report evidence showcased till date on SG. SG references from ancient ayurvedic writings, such as Charak Samhita, Sushrut Samhita, Astang Hridyam, among others, have been gathered. The many techniques of preparing same medication are examined critically. Probable mode of action of SG in non-alcoholic fatty liver understood after critical analysis of various studies (clinical and experimental). Ketone formation occurs during Snehpana, which inhibits de novo lipogenesis and promotes fatty acid oxidation, resulting in weight loss and decreased hepatic fat content. Evidence indicates that ketones play a protective role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD). It can be concluded that Snehpana with Shatpala ghrit can be beneficial in reversing the stages of NAFLD.

Keywords: Shatpala ghrita, Snehpana, Lipid Based Drug Delivery System, NAFLD, Ketogenic diet

INTRODUCTION

Among the various preparations described in Ayurvedic texts, such as Panchavidha Kashaya Kalpana (Swarasa, Kalka, Kwatha, Hima, and Phanta), medicated lipids (Sneha Kalpana) can be considered a form of Lipid-Based Drug Delivery System (LBDDS). This is because the process of preparing oleaginous formulations involves using basic herbal dosage forms like paste, juice, and decoctions, along with other liquid mediums, such as milk, water, and buttermilk. These ingredients are combined in specific proportions and subjected to heat (sneha paka) until the water content is fully evaporated [1]. This process ensures the uniform distribution and absorption of both fat-soluble and water-soluble chemical constituents. The final stage of production is specific to oils and ghee (paka siddhi), where the residual material is heated over a flame to ensure complete water evaporation, indicated by the absence of any crackling sound. Additionally, Murchhana, or the fortification of lipids with certain herbs, is recommended to enhance solubility and absorption, eliminate moisture that could cause rancidity (amadosha) and unpleasant odors, and improve the color and fragrance of the oil or ghee [2].

The active bioactive compounds are transferred into lipid solvents, such as sesame oil and cow's ghee, which are then used for various routes of administration, including oral (paan), nasal

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instillation (nasya), dermal (abhyanga), per rectum (enema), and topical applications [1]. Cell membranes are mainly made up of a bilayer lipid matrix, which influences the permeability and specificity of drug molecules. Lipid-based drugs are more readily absorbed as they passively diffuse across the cell membrane at a faster rate [2]. Recently, Lipid-Based Drug Delivery Systems (LBDDS) have demonstrated effective size-dependent properties, addressing the challenges associated with the solubility and bioavailability of poorly water-soluble drugs. This system offers superiority due to its clear advantages in biocompatibility and versatility. Ayurvedic lipid formulations vary widely, ranging from single to polyherbal combinations, single lipid to mixed lipids, with or without milk, and involving single or multiple cycles of drug enrichment (avartana). These variations allow for flexibility in meeting diverse product requirements based on disease conditions, administration routes, cost, stability, safety, and efficacy [3].

There are notable reports on the use of lipid-based formulations in the treatment of various chronic and life-threatening diseases. Shatpala ghrit (SG) has potential for clinical applications. Previously no clinical and animal studies data report is evidence till date on SG. SG has been ascribed to in classical texts. Among them, all are administered for various diseases and conditions. It is recommended in several disease conditions like Grahani Udara (disease of abdomen), Gulma (abdominal lump), Pliha (Splenic disease), Jwara (Fever), Kasa (Cough), Svasa (Dysponea/Asthma), Pandu, Pratishyaya (Chronic rhinitis or sinusitis), Svayathu (Oedema), Agni sanga (Impaired digestive fire), Udavart, Vishama jwara, Urdhwa vata, etc. [2].

Shatpala ghrita references from ancient ayurvedic writings, such as Charak Samhita, Sushrut Samhita, Astang Hridyam, among others, have been gathered. The many techniques of preparing same medication are examined critically. Methods of preparation of Shatpala is described in Table 1 & details of Shatpala ghrit are mentioned in Table 2.

WHAT IS SNEHPANA?

SP is an intake of fat orally. It is categorized into 3 categories.

The first one is used for shodhan (as poorva karma) and is called madhyam matra. Fat is taken early in the morning in testing dosage of approx. 30 ml on first day and then progressively dose is increased according to the appetite for minimum 03 days to maximum 07 days (depending upon symptoms of proper snehpana). Then food is taken after sensation of huger in 1/3 less quantity than usual diet (liquid, easily digestible, hot). Various diseases described where this can be given like Prameha Pidika (Diabetes mellitus complications), Skin disease, vata-rakta, etc. Various properties are also explained as bahudoshe.

Bahu Matra after Digestion of Evening Diet

The second category is used as Shaman sneha and named as Pradhan matra. It is given in high dosage and takes 24 hours to digest. It is described in Gadha mutra-varcha, gar-visha,

After Hunger & Without Taking Meal

Third category is called Brimhana snehana. It is used in Chronic kasa, jwara and atisara. It is used in with meal/eatable in less quantity/very low dosage.

Ayurvedic classification of snehpana dose is time specific (depending upon time for digestion, i.e., 2, 4, 8 yama).

CORRELATION OF SP WITH KD

Snehpana is like a ketogenic diet (KD) practiced in today’s era. It is widely accepted that a ketogenic diet (KD) contains very low carbohydrate levels, typically 5–10% of the total daily caloric intake, amounting to 50–20 grams per day. A ketogenic diet induces ketogenesis, a metabolic process that produces ketone bodies – acetoacetate, beta-hydroxybutyrate, and acetone – which serve as alternative fat-derived fuel for essential organs during periods of nutrient scarcity (such as after deepan-pachan, light food intake, or hunger). The production of ketone bodies is referred to as ketosis. Like a ketogenic diet (KD), ketosis is also induced after snehpana. Ketosis occurs when carbohydrate intake is reduced to less than 50 grams per day, with either restricted or unrestricted fat and calorie consumption. The same effect is observed during snehpana. Ketones play a role in reducing inflammation and addressing the metabolic complications associated with the pathogenesis of non-alcoholic fatty liver disease (NAFLD) [4].

Table 1. Description of the contents of Shatpala ghrit.

Ingredients	Scientific Name	Part Used	Rasa	Guna	Virya	Vipaka	Dosh	References	Pharmacological Activity
Pippali	Piper longum	Fruit	Katu	Laghu SnigdhaTikshan	Anusna-sheet	Madhur	Vata-kapha shamak	Bhav prakash purva khand haritakiaadi varga (49–54)	Appetizer and digestive effects, relieve constipation
Pippali moola	Piper longum	Root	Katu	Laghu Snigdha Tikshan	Anusna sitt	Madhur	Kapha-vaat har	Bhavprakashpurvakhandharitakiaadivarga (54)	appetizer and digestive effects
Chavya	Piper chaba	Stem	Katu	Laghu RukshaTikshan	Ushna	Madhur	Kapha-vaat samak	Bhavprakashpurva khand haritakiaadi varga (61)	Anti-inflammatory activity Digestive and appetizing property, In piles, constipation, abdominal lump, abdominal and splenic diseases
Chitraka	Plumbago zeylanica	Root bark	Katu	Laghu Tikshan	Ushana	Katu	Kaphavaatshamak	Bhav prakash purva khand haritakiaadi varga (64)	Digestive& carminative herb effect, Used in Grahni, Udara, kustha, Sotha, Svasa, Obesity, Asthma, Diarrhea
Shunthi	Zingiber officinale	Rhizome	Katu	Laghu Snigdha Ruksha Tikshan	Ushna	Katu	Kapha-vaat har	Bhav prakashpurvakhand haritakiaadiv arga (41–45)	Anti-inflammatory property, Hepatoprotective activity, Gastroprotective activity, cardio protective effect, Anti atherosclerotic activity
Yavakshara	Hordeum vulgare	Fruit	Madhur Tikt. Kashaya	Ruksha Picchil Mridu Anabhisyandi	Sitt	Katu	Vaat-kapha har	Bhav prakash purva khand haritakiaadi varga (219–221)	Abdominal pain, bloating, etc. Used as pathya in diabetes, obesity, and heart diseases. Laxative effect

Before snehpana, nutrient deprivation stage is created via deepen pachana (fasting, glucose deprivation, and prolonged physical exercise). Then snehpana provides fat as metabolic fuel and causes ketogenesis. Also, carbohydrates are restricted during snehpana as in KD. The relationship of division of sneha doses and categories of researched KD are shown in Table 3.

Table 2. Details of Shatpala ghrit mentioned in Ayurvedic texts.

Samhita	Reference	Rogadhikar	Contents	Indications
1. Charak	Ch.Chi 5/147-148	*Gulma*	*Pippali (1 pal), Pippali mool (1 pal), Chavya (1 pal), Chitrka (1 pal), Sunthi (1 pal), Yavakshara (1 pal), Milk (1prastha), Goghrit (1 prastha)*	*Kaphaj Gulma, Grahni, Pandu, Pleehavridhi, Kasa, Jvara*
	Ch.Chi 13/112-114		*Pippali(half pal)Pippalimool (Half pal), Chavya (Half pal), Chitrak (half pal), Sunthi (half pal), Ghritt (2 prasth) Panch-mool svaras (half hoola), Dadhimastu (1 aadhak)*	*Sotha, Vatajanya vistambh, Gulma, Arsh*
2. Sushrut	Su.Chi 14/14	*Udara*	*Pippali (1 pal), Pippalimool (1 pal), Chavya (1 pal), Chitrka (1 pal), Sunthi (1 pal), Yavakshara (1 pal), Sendha namak (1 pal), Ghrit* (1 *prastha), Dugdh* (1 *prastha)*	*Pleeha, Agni mandya, Gulma, Udar rog, Udawart, Urdhavvaat, soth, Paandu Kasa, Svasa, Pratishyay, Visham jvara*
3. Astang hridyam	A.H.Chi 5/22-23	*Rajyakshma*	*Panchkol (1–1 pal) Yavkshar (1 pal) Ghrit (1 prastha) Dugdh (1 prastha)*	*Gulma*, Jwar, Udar rog, Pleeha Grahni, Urdhav vaat, Pandu, Kasa Shvaythu, Agni mandya, *Sroto-shodhan*

Table 3. Coorelation of sneha doses and KD.

Researched Categories of KD					Ayurvedic Categories			
	Kcal/Day	**CHO/Day**	**Fat/Day**	**Purpose (Ketosis)**	**Purpose**	**Fat**	**CHO/Day**	**Kcal/Day**
HFKD	unrestricted	<20–50 g	Unrestricted	yes	Shodhanartha sneha	Approx. 1890–2160 cal or Bahu matra (~unrestricted)	<20–50 g	unrestricted Uncertain as it varies from person to person)
VLCKD	<800 Kcal	<20–50 g	Low	yes	Shaman sneha	270 cal-720 cal (moderate dose)	<20–50 g (or protein-80 cal can be taken)	370 cal-800 cal
VLCD	<800 kcal	>20–50 g	Low	usually not	Brimhgana sneha	Very less quantity	–	–

HFKD AND AYURVEDIC SNEHPANA MATRA

As snehpana, High fat KDs (HFKD) are administered. Ketogenic diets (KDs) are typically defined by a carbohydrate restriction of less than 50 grams per day, with an unrestricted intake of fat (like the progressive dosing of snehpana), a moderate increase in protein intake (0.8–1.2 g per day), and ad libitum caloric intake. However, the satiety effects of diet often naturally limit overall calorie consumption [2].

HFKD (High-Fat Ketogenic Diet) involves a carbohydrate intake of less than 20–50 grams per day and may be mildly hypocaloric, normocaloric, or unrestricted, with a gradual increase in fat content. Similarly, in snehpana, fat intake is progressively increased in conjunction with the diet, tailored to the individual’s appetite and condition (purusham purusham vikshaya).

In shodhartha sneha, diet mentioned is drava, ushna, anabhishyandi, naati-snigdha, asankara. Diet may be 1 piece of bread (~roti/phulka) [25 g x 4 cal = 100 cal] or 1 cup cooked rice [30 g x 4 = 120 cal]. with 1 cup of pulses in liquid and processed form [100 ml x 4 = 400 cal]. On the first day sneha dose is approx 30 ml (30 x 9 = 270 cal). So minimum calories of the first day may vary approx between 770 cal to 890 cal (vary person to person). In this way, with each day, fat quantity is increased to 7 days. In various research maximum doses decided till the 7th day was 210 ml (~1890 cal), 240 ml (~2160 cal) and total amount of snehpana daily per person range from 400–1050 ml.

Shodhanartha Snehpana Dose and KD

In ayurvedic perspective, in laghu triyi and post texts doses and diet are described pattern (Dosewise/daywise/according to koshtha) (Table 4).

The European Food Safety Authority (EFSA) defines very low-calorie diets (VLCDs) as ketogenic when they contain 1.2–1.4 g of protein per kilogram of ideal body weight (approximately 75 g per day), a very limited carbohydrate intake (<30–50 g/day, <5–10%), a fixed amount of fats (20 g/day, 15–30%, primarily from olive oil), and sufficient micronutrients to meet the Dietary Reference Intake. This fact can reinforce the content of shaman sneha in NAFLD carrying dominance of vata/locomotor system disease dominant in vata.

Table 4. Day wise Sneha doses according to acharya Vangsen.

	1st	**2nd**	**3rd**	**4th**	**5th**	**6th**	**7th**
Uttam	3 pal	31/2 pal	4 pal	4 n half pal	5 pal	5.5 pal	6 pal
Madhyam	1½ pala	7karsha	8 karsha	9 karsha	10 karsha	11 karsha	3 pala
hrishawa	3 karsha						6 karsha

Table 5. Shaman Snehpana Dose and KD Calories.

Acharya	**Dose**	**KD Calorie**
Vangsena	1½ pala/60 ml	60 x 9 = 720 cal
Chakrapani	3 karsha/30 ml	270 cal
Sharangdhara	3 karsha/30 ml	270 cal
Bhavprakasha	3 karsha/30 ml	270 cal
Dr. H. S. Kasture13	6 tola (60 ml in 3 dose)	720 cal

In shaman sneha, diet advised as regime followed after virechana, i.e., Sansarjana karma.In sansarjana karma, diet in sequence is taken as – peya (rice water), vilepi (~ rice semisolid soup), Akrut yusha (unprocessed soup of pulses), krut yusha (processed soupy pulses), unprocessed akrut mansa ras/urad dal, processed mansa ras. It can be understood in another opinion, i.e., diet should be according to appetite. If appetite is low, then liquid diet (rice water (20 ml x 4 = 80 cal)/mudga yusha of (100 ml x 4 = 400 cal). If appetite is moderate then sometime liquid and sometime semisolid (Vilepi ~ rice soup, Krut yusha, etc.). If appetite is good, then solid content can be taken (Mansa ras/Urad dal (150 g x 4 = 600 cal)/Rice (120 cal) or all (Table 5).

Low-carbohydrate diets (LCDs) are typically defined as those containing less than 130 grams of carbohydrates per day. In 1863, William Banting, an obese former English undertaker and coffin maker, introduced the low-carbohydrate diet (LCD) in his publication Letter on Corpulence Addressed to the Public. In this letter, he outlined a weight-loss regimen that eliminated bread, butter, milk, sugar, beer, and potatoes. More recently, the American Diabetes Association has affirmed that LCDs aid in weight loss and improve blood glucose levels and lipid profiles in individuals with type 2 diabetes mellitus (T2DM). LCDs do not necessarily fall into the category where ketosis occurs because KDs are diets with a CHO content of less than 50 g, whereas LCDs have one of 50 to 130 g/day. LCDs can be correlated with Brimhgan sneha; however, this is not explained here because it is not as pertinent to the topic. Based on the information above, it can be concluded that Snehpana functions in a manner like ketogenic diets, as both involve processes that promote ketogenesis, reduce carbohydrate intake, and help in managing conditions like obesity and metabolic disorders.

HOW KETOSIS DEVELOP THROUGH SNEHPANA?

Prior to snehpana, the body produced a ketogenesis stimulus through deepan pachan. During times of low glucose availability, fatty acids are released from adipose tissue due to signaling from high levels of glucagon and epinephrine, as well as low levels of insulin. These fatty acids undergo β-oxidation in the hepatic mitochondrial matrix to produce acetyl-CoA, where ketogenesis occurs. Under normal conditions, the citric acid cycle (TCA/Krebs cycle) and the mitochondrial electron transport chain work together to oxidize acetyl-CoA, generating energy in the process. During times of prolonged fasting, glucose deprivation, and intense physical activity, excess amounts of acetyl-CoA from fatty acid β-oxidation are redirected towards the production of ketone bodies when the TCA cycle is unable to keep up with the demand (deepan-pachan-means to achieve rukshan).

Specifically, the body uses two ketones for energy: acetoacetate and β-hydroxybutyrate. Following their return to acetyl-CoA in extrahepatic organs, they undergo the TCA cycle and oxidative phosphorylation, which yields 22 ATP molecules per unit. Acetone is either inhaled or eliminated through urine since it cannot be changed back into acetyl-CoA. According to physiological principles, the human liver produces up to 300 g of ketones each day during ketosis. The production of ketones is regulated by a complex biochemical and hormonal system that controls their timing, rate, and speed. This process can vary depending on the intensity and duration of the ketogenic stimulus. The daily increase in fat content during snehpana intensifies the stimulus [5]. Studies showing KD effect in NAFLD.

EFFECT ON GENE LEVEL

Additionally, ketones are believed to act as both direct and indirect epigenetic modifiers of key histones, which play a dynamic role in regulating chromatin structure and gene expression. Shimazu et al. found that β-hydroxybutyrate (βOHB) enhanced global histone acetylation, leading to transcriptional changes in mouse models, including the upregulation of genes involved in oxidative stress resistance. This suggests that βOHB may help promote resistance to oxidative stress [5]. Furthermore, βOHB is a naturally occurring activator of GPR109A, which is highly expressed in various immune cells, including macrophages and monocytes. The anti-inflammatory effects of GPR109A ligands have been observed in conditions, such as atherosclerosis, obesity, inflammatory bowel disease, neurological disorders, and cancer [6].

βHB has also been associated with the inhibition of inflammasomes, particularly NLRP3, a crucial signaling platform that activates proinflammatory cytokines, such as IL-1β and IL-18, which are closely linked to obesity and the development of insulin resistance (IR) and type 2 diabetes mellitus (T2DM). Interestingly, increasing evidence suggests that NLRP3-induced pyroptosis plays a central role in mouse models of liver fibrosis.

EFFECT ON MITOCHONDRIA

A ketogenic diet for 6 days significantly reduced liver fat content and improved hepatic insulin resistance. These changes were linked to an increased breakdown of liver triglycerides, along with a reduction in endogenous glucose production and serum insulin levels. The shift of fatty acids towards ketogenesis increased, which correlated with an enhanced hepatic mitochondrial redox state and reduced hepatic citrate synthase activity. These findings reveal previously unrecognized adaptations that contribute to the reversal of NAFLD through a ketogenic diet, emphasizing hepatic mitochondrial fluxes and redox state as potential targets for NAFLD treatment [3].

PREVIOUS STUDIES SUPPORTING THIS FACT

It is commonly believed that increased dietary fat intake continuously leads to fatty liver; however, several studies have recognized that traditional ketogenic diets (KD) improve the hepatic lipid profile and help alleviate non-alcoholic fatty liver disease (NAFLD). In fact, Luukkonen et al. investigated the impact of a 6-day ketogenic diet (KD) on hepatic steatosis and observed a reduction in liver fat content and hepatic insulin resistance in NAFLD patients. Another study on NAFLD patients showed improvements in steatosis, necroinflammation, and fibrosis after following a ketogenic diet for 6 months. Additionally, a 2-week ketogenic diet intervention in obese NAFLD patients resulted in a simultaneous reduction in de novo lipogenesis (DNL) and liver fat. When NAFLD patients followed a Spanish ketogenic Mediterranean diet for 12 weeks, significant improvements were observed in their steatosis score, AST, and ALT levels. Another study involving 24 obese patients on a very low-calorie ketogenic diet for 6 months demonstrated notable improvements in serum liver function markers and triglyceride levels. Although ketogenic diets offer several benefits, some studies have raised safety concerns, especially with high-fat content. For instance, patients on a very low-calorie ketogenic diet experienced elevated serum cholesterol levels and increased liver function markers, such as AST and ALT.

Recently, intermittent fasting, a potent inducer of ketogenesis, has gained attention for its effectiveness in treating NAFLD patients. Various forms of intermittent fasting, such as time-restricted fasting, periodic fasting, or calorie restriction, have been shown to significantly reduce liver lipid accumulation and improve biochemical liver function markers, including AST and ALT levels [7].

Tendler et al. recruited five obese patients with a histological diagnosis of NAFLD and placed them on a calorie-unrestricted high-fat ketogenic diet (HFKD) for 6 months. Along with an overall weight loss of 10.9%, four out of the five patients showed improvements in steatosis, necroinflammatory grade, and fibrosis by the end of the study [8].

In another 12-week prospective study, 14 overweight male patients with metabolic syndrome and ALT levels above 40 IU were prescribed a Mediterranean high-fat ketogenic diet (HFKD), unrestricted in calories and rich in unsaturated fats like omega-3 fish oil and extra virgin olive oil. By the end of the study, there was a significant improvement in body weight, aminotransferase levels, and ultrasound-derived steatosis degree. Complete fatty liver regression was observed in 21.4% of patients, and an overall reduction was seen in 92.86% of the patients [9]. Similar outcomes were observed in a cohort of 27 patients with morbid obesity (body mass index [BMI] of 45.2 kg/m^2), where ultrasound-measured hepatic lobe volume decreased by 19.8% after 4 weeks of pre-bariatric high-fat ketogenic diet (HFKD) at approximately 1250 kcal/day (4% carbohydrates, 71% fat, 25% protein) [4].

Mardinoglu et al. conducted a 2-week intervention with a high-fat ketogenic diet (HFKD) (3115 kcal/day, 20–30 g carbohydrates/day, 241 g fat/day) in 17 patients diagnosed with obesity and NAFLD. Although there was minimal weight loss, a significant reduction in liver fat, assessed by magnetic resonance spectroscopy (MRS), was observed, along with a corresponding decrease in the expression of genes involved in hepatic de novo lipogenesis

Kirk et al. conducted a randomized controlled trial (RCT) with 22 obese subjects, comparing a high-fat ketogenic diet (HFKD) (75% fat; <60 g carbohydrates/day, approximately 10% of daily intake) to a low-fat high-carbohydrate (LFHC) diet (20% fat; >180 g carbohydrates/day, approximately 65% of daily intake) on a hypocaloric regimen (1000 kcal daily energy deficit, based on estimated daily energy needs). After 48 hours, intrahepatic triglyceride content decreased more significantly in the HFKD group than in the LFHC group (29.6 ± 4.8% vs. 8.9 ± 1.4%; $p < 0.05$). However, after 11 weeks, when both groups achieved a 7% weight loss, the reduction in intrahepatic triglyceride content was similar in both groups (38.0 ± 4.5% for HFKD vs. 44.5 ± 13.5% for LFHC).

Another 30-day prospective study involving 50 obese individuals preparing for bariatric surgery found that a sequential diet, including a 10-day very low-calorie ketogenic diet (VLCKD) (15 g carbohydrates/day), resulted in improved liver steatosis and an average 30% reduction in hepatic volume [10].

Similar findings were observed in a study involving 32 obese patients who followed a very low-calorie ketogenic diet (VLCKD) (45 g carbohydrates/day) for 12 weeks. By the end of the study, CT and MRI scans showed a 28.7% reduction in liver size, with 80% of this reduction occurring during the first 2 weeks.

In line with these findings, another study comparing VLCKD with simple dietary counseling demonstrated better outcomes, including a greater reduction in liver steatosis as assessed by ultrasound and a decrease in GGT levels.

All these studies indicate that ketogenic diets have beneficial effects on NAFLD, which can also be assumed for snehpana.

MECHANISM FOR IMPACT IN NAFLD

Non-alcoholic fatty liver disease (NAFLD) is characterized by excessive fat accumulation in the liver, not associated with significant alcohol consumption. The mechanisms underlying its impact involve a multifactorial interplay given in Figure 1.

Snehpana, like the ketogenic diet, may help protect against NAFLD through various mechanisms. First, like the KD, Snehpana induces a metabolic state akin to fasting, leading to weight loss and improvements in metabolic balance. Secondly, the anti-steatotic effects are attributed to the hydrolysis of hepatic lipids and their diversion toward the ketogenic pathway, which results in lower serum insulin levels and reduced hepatic citrate synthase flux. The ketogenic diet activates PPARα, a key downstream target of FGF21, enhancing fatty acid β-oxidation. A similar effect might occur with snehpana.

Third, like the ketogenic diet, Snehpana reduces hepatic de novo lipogenesis (DNL) and fatty acid synthesis by inhibiting stearoyl-CoA desaturase activity. Fourth, like the KD, Snehpana enhances mitochondrial biogenesis and function by upregulating the expression of peroxisome proliferator-activated receptor γ coactivator 1α (PGC1α) in the liver. At the central level, Snehpana (SP), like the ketogenic diet (KD), influences satiety, resulting in reduced food consumption. Like KD, SP may also mitigate oxidative stress and inflammation by inhibiting NLRP3, activating G-protein-coupled receptors (GPRs), and promoting histone acetylation. Therefore, SP, akin to KD, when implemented through calorie restriction and specific macronutrient distribution, has the potential to effectively manage NAFLD. However, the precise mechanisms underlying these effects in the context of SP require further exploration. Given the similarities between SP and KD, it is reasonable to infer that the mechanisms influenced by KD could also apply to SP (Figure 1).

A central mechanism driving many of these positive effects seems to be the body's preferential shift from glucose derived through glycogenolysis to ketones produced via lipolysis. Substantial evidence highlights the hepatoprotective benefits of this shift, particularly in addressing obesity and metabolic syndrome. NAFLD, which reflects excess body fat in the liver, has been associated with insulin resistance, elevated oxidative stress, and inflammation, often leading to significant fibrosis. To begin with, ketogenic diets (KDs), due to their extremely low carbohydrate content, lead to a reduction in insulin levels. This decrease subsequently suppresses lipogenesis while enhancing the rate of fatty acid oxidation [11]. Recent studies indicate that a significant reduction in dietary carbohydrates triggers a shift in gut microbiota composition, which enhances folate production. This, in turn, improves lipid metabolism while reducing oxidative stress and inflammation [12].

A normocaloric high-fat ketogenic diet suppresses de novo lipogenesis and promotes fatty acid oxidation, resulting in weight loss and a reduction in liver fat content [13]. In contrast, a hypercaloric balanced diet reduces intrahepatic fatty acid oxidation while enhancing de novo lipogenesis, predominantly from carbohydrate sources rather than lipid substrates, contributing to the onset of NAFLD. Additionally, ketone esters have been given to athletes, promoting muscle fat oxidation and reducing glycolysis, even without adhering to a carbohydrate-restricted diet. In summary, the collective evidence indicates that ketones may play a protective role in the development of NAFLD, potentially extending beyond the effects of mere weight loss.

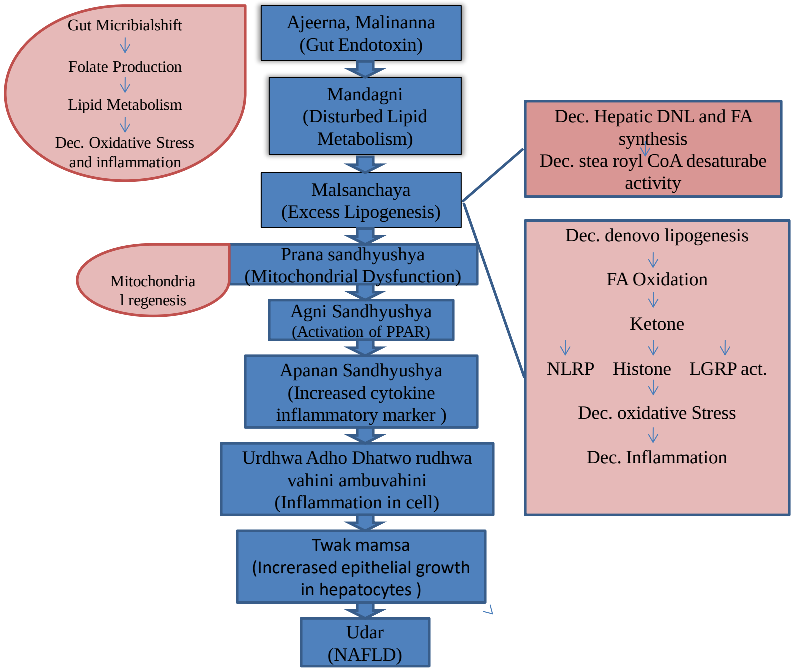

Figure 1. Mode of action of Snehpana in NAFLD.

AYURVEDIC PERSPECTIVE

Liver is the organ responsible for metabolism. Liver profile is disturbed by liver disease which indicate the inflammation of heapatocyte, breakage of cells due to deposition of fat (srotorodha). This led to marg avrodha in inward movement and outward movement of anything required for cell. Also, Apana dusti is present as toxins produced as a result of cycles, are not excreted out due to fat deposition which led to mala vridhi and dosha sanchaya (free fatty acids) as described in pathogenesis of disease. Yakrut is sathan of raktavah srotas. If disease happen in this site than treatment of Raktvaha srotodushti will be there. Rakta resembles with pitta in many terms. Pitta is treated with sanshaman, upvas, raktmokshan and virechana. Likewise, there will be treatment of raktavaha srotodusti due to similarities between pitta and raktavaha. In case of NAFLD, MAFLD (diseases prevalent in this era of disturbed and faulty lifestyle), Virechana can be adopted for srotoshodhan and Agni deepti. Since in this disease of medovaha srotodusti in liver (fat deposition in liver cells), it was doubt/possibility that sneha may promote the progression of disease but researches carried out in NAFLD where Ketogenic diet usage (fat used abundantly with partial restriction of carbohydrate and diet) resulted in decrease in steatosis/fat deposition, improvement in LFT (detailed in Table 5). Beside this, special kind of drugs are mentioned in such kind of diseases where shodhan is required but because of disease pathology, clinician restrict themselves avoiding usage of snehpana. To overcome this limitation, shatpala ghrit is mentioned as it is having contents of Panchkola and sajjikshar which carries property of deepan-pachan, srotoshodhan at level of dhatvagni. Because of ghrit, fat soluble toxins get mixed and purification–detoxification can be achieved. Also, Ghritthas has unique property of pacifying the vitiated vata and pitt dosh. Also Agni dipan action means stimulate the digestive enzyme to increase appetite digestion and absorption. Modern research have proved that lipid-based formulations are more efficient career for the drug delivery to target organ system. Through SP, ketones formation increases which helps in reversal of disease as detailed further.

Before snehpana, samyak deepan pachan (Grathita purisha, Ruksha body, Durbalata, Mand-agni, difficulty in digestion, burning in chest/thoracic region, etc. (SU.CHI) is highly required. If patient has vata dominant symptoms like Parvbheda (joint pain, backache), kostha shula (pain abdomen), udavarta (incomplete evacuation, difficulty in passing stool and vata), anaha (abdominal distension), disturbed sleep, etc. then snehpana can be administered. In paittika condition (daha, moha, increased thirst, jwara (feeling feverish), virechana is required so before that, snehpana can be done. In case of Kapha, guruta (heaviness), aruchi (severe loss of appetite/interest in food) and kathnaya (atherosclerosis, condition of disturbed lipid profile) is there so caution is needed before snehpana.

Grade I FL can be considered as madhyam avastha of dosha along with Raktvaha-mansvaha srotodushti [Sanga, vimarg-gaman (Fatty acid/triglyceride deposition is done in adipose tissue but it gets accumulated in liver and that also in excessive/great extent (Atipravriti)]. In madhym avastha of dosha, deepan-pachan can help to a great extent. In this condition, to prevent further progression/reoccurrence, shodhan can be planned.

Grade II FL can be considered as Bahu Doshavastha along with srotodusti of srotas of grade I (vimarg-gaman and granthi (development of atherosclerosis, CVD). In bahu dosh-avastha, shodhan is a must. For shodhan, medications mentioned in udara vikara need to be used for proper management.

In these above conditions, Snehpana can be used without fear of progression/deposition of extra fat in liver if proper deepan-pachana and rukshana can be achieved. Secondly, Ghrita does deepen and increase agni without digesting Ama. Ama is already pathology in NAFLD and for *Ama-pachan, Panchkola, Yavkshar, Hingu, sendha namak*, etc. are there. So, combination of these drugs with ghrit does collaborative effect of Deepan-pachan without aggravating the condition and impacting good effect. DP effect of SG helps it to reach cellular level and help in Vishyandan of dosha (~toxins) by going to deeper level. Also, DP is given prior as Snehpana can help slight blockage done by fat deposition (of level grade I, II). But stage can progress, so to prevent it from root/recurrence/progression, shodhan is planned after proper snehpana.

If condition of Mandagni and krur kostha exists, snehpana is to be done. Ghrit mixed with kshar, lavan (as in SG) & after proper snehana-swedana, virechana can be administered (SU.CHI.).

After shodhan, as a rasayan in all udara vikara or disease carrying similar pathogenesis can be utilized.

Like ketogenic diet, if there is condition of decrease in protein level in blood (hypoalbuminaemia, etc.) then it needs to be avoided to go for snehpana or given with supplementation of some protein in diet (after sneh digestion, diet given of mudga yusha).

CONCLUSIONS

Considering all the above facts, it can be understood that Shatpala ghrit (prescribed in spleen and liver related condition according to ayurveda) is beneficial in NAFLD. Contents of Shatpala ghrit also help in reversing the stages of fatty liver. Altogether, these data suggest that both caloric restriction and macronutrient distribution play a role that.

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