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Review

Obesity and Non-Alcoholic Fatty Liver - Therapies in Ayurvedic Medicines

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Abstract:

Ayurveda is an ancient Indian medicinal practice. The present review includes translational research characterizing obesity, non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH).

We reviewed published research on improving function through Ayurvedic medicine by searching electronic databases (Medline, Embase) using terms such as: Ayurveda, obesity, NAFLD, NASH, the effect of exercise interventions in obesity, change in body composition. We aim to (1) determine the immuno-pathology of liver damage due to imbalance in diet and life style, (2) examine the role of behavior in the development of obesity and NAFLD-NASH. Special accent is put on Ayurveda recommendations.

Keywords

Ayurveda; Body mass index; Behavior; Diet; Non-alcoholic fatty liver; Nonalcoholic steatohepatitis; Obesity; Exercise

Ayurveda has been practiced for over 5000 years in the Indian subcontinent ever since the ancient Indus Valley Civilization. Its roots are in traditional Hindu healthcare system. Ayurveda name comes from Sanskrit language “ayur”-life and “veda”-knowledge. The focus of its practice is on natural medicines and exercises (yoga) to maintain balance in the human body. It promotes the use of herbal diets for general wellness practices and medicinal uses. Older generations in India have always preferred the use of Ayurvedic treatments compared to any other modern medicinal practices. Ayurvedic medicine has gained popularity, as integrative medicines are being preferred over pharmaceutical medications. Patients often seek non-traditional forms of treatment including alternative medical options go meet their personal needs, as they are thought to be safer.

Ayurveda uses esoteric knowledge of the Vedas, ancient scriptures from India, to heal illnesses by practicing yoga, massages, and ingestion of herbs, spices, and roots that contain medicinal ingredients to cure any sort of illnesses and maintain general well being. Not only is Ayurveda popular in India but also is on the rise on all parts of the world as holistic, traditional, and herbal medications are thought to be not harmful compared to synthesized medications. Ayurveda plays a role in establishing natural practices to avoid obesity and NAFLD.

In United States and Canada interest has grown in methods to reduce obesity and improve liver function through Ayurvedic medicine. However, Ayurvedic products sold over the Internet or in stores may contain levels of lead, mercury and arsenic that exceed standards for acceptable daily intake [1].

Obesity is one of the major health problems that the world is battling today due to populations experiencing more stress, sedentary lifestyles, lack of balance in professional and personal life. The World Health Organization (WHO) concluded in 2016 report that worldwide obesity has doubled from 1980. There are 1.9 billion adults are either overweight or obese. In 2014, 41 million children under the age of 5 were obese, 39% of adults were overweight, while 13% were considered obese [2].

Obesity leads to various other diseases such as metabolic syndrome, non-alcoholic fatty liver disease, and liver cirrhosis [3, 4]. Lipotoxicity leads to cellular injury and stimulation of the inflammatory responses and fibrogenesis. Cytokines activate many signaling cascades that regulate fibrogenesis.

Adipocytes forming the adipose tissue are highly active metabolic endocrine cells, which produce various cytokines. Adipose tissue-derived cytokines or adipokines are involved in the regulation of many processes such as energy metabolism, inflammation, diabetes and atherosclerosis [5]. Indeed, increased levels of adipokines and pro-inflammatory cytokines, such as leptin, adiponectin, resistin, apelin or visfatin, tumor necrosis factor-alpha (TNF-α), and interleukin-6, have prominent roles in the pathogenesis of the metabolic syndrome [6]. Leptin and adiponectin both are associated with regulation of energy balance and insulin action and obesity negatively affects the levels of these molecules. Leptin also promotes body mass loss decreasing food intake and increasing sympathetic

nervous system activity through the hypothalamus. Furthermore, adiponectin has anti-atherogenic, anti-diabetic and anti-inflammatory properties and also play an essential role in maintaining homeostasis in the human body. Resistin is produced by white and brown adipose tissues and is elevated in obesity [5]. There is growing evidence emphasizing a role of resistin as a pro-inflammatory adipocytokine in humans [6], while visfatin contribute to vascular disease by inducing endothelial dysfunction through a variety of mechanisms [7, 8].

Regular exercise that is also promoted by traditional Indian medicine has been shown to result in positive adaptations and act as adjuvant for obesity prevention and treatment. In addition, regular exercise can potentially modify metabolic hormones and is considered an important treatment of chronic inflammation and obesity-related conditions. The magnitude of benefits may vary with the type and amount of exercise. A systematic review and meta-analysis of 14 clinical trials in adults with type 2 diabetes showed that an aerobic exercise program was associated with a significant reduction as follows: CRP from baseline levels (-14%), interleukin-6 (IL-6) -18% and leptin -24% . However, it did not change the levels of adiponectin or resistin [9]. Furthermore, in pediatric obesity, exercise has an impact on the adipose tissue and the release of adiponectin, resistin, and visfatin [10, 11].

Traditional medicine attempts to provide patients with evidence-based therapeutic regiments for their condition. Integrative medicine or complementary and alternative medicine is used to prevent and to manage the problems associated with obesity and fatty liver. Due to rise of interest in natural medications, the following research review considers current researches on Ayurveda's spices, roots, herbs, plants, fruits, natural ingredients, and lifestyle therapies that can be used in treatment of obesity and fatty liver disease.

To understand the classical texts about curing obesity, one must understand the meaning of concepts: "kapha, pitta, and vata" which are Ayurveda doshas that represent the qualities of nature. The doshas are energies in the body that govern all mental and physical processes. The five elements are space, air, fire, water, and earth. Vata reflects the elements of space and air, Pitta reflects the elements of fire and water, and kapha represents the elements of water and earth. All kinds of food can be represented by these three doshas.

Kapha characteristics are cold, heavy, sticky, and lethargic. Pitta characteristics are sharp, hot, acidic, and moving. Vata characteristics are dry, rough, light, and mobile. In order to maintain a healthy balance diet, kapha, pitta, and vata must be balanced. In Sanskrit adipose tissue is called meda and obesity is known as medo roga. Adipose is caused by disequilibrium consumption of kapha foods. Kapha foods are cold, sweet, oily, and fat [12]. Medas are associated with as due to abundance, heaviness, and a radiating nature. According to Caraka Samhita, one of the volumes of Ayurveda's classical texts, obesity is caused by excess consumption of kapha, day-time sleeping, lack of physical and mental work, and genetic defects [12]. Inactivity or loss of physical activity can be caused as adipose tissue, which has characteristics of kapha is heavy. This can lead to further hunger and increase in thirst. The classical verse describes the cause of obesity caused by excess Vayu and Agni [12]. Vayu is wind, whereas Agni is fire. The cosmic "fire" is responsible for digestion, whereas the wind aids in absorption and digestion through extinguishing the fire. Adipose tissues can block wind's passage to the abdomen and these results in fire being intensified leading to accelerate digestion process leaving the body hungry faster. In order to reduce obesity, one must consume Vata

foods relating to Vayu in order to decrease kapha [12]. Foods flavors that increase Vata are pungent, astringent, and bitter. According to Caraka, increasing Vata foods, increase in mental and physical work, and ensuring proper night-time sleep will aid in reduction of adipose tissues. According to the Ayurveda texts, the following list describes the etiology of obesity [13]: avyayama (no exercise), diva swapna (day time sleep), avyavaya (no sexual intercourse), achinta (no worries), prameha poorva rupa (prodromal signs), beej-dosa (genetic problems), agni-mandaya (no appetite), meda-vrittavayu (lipo-toxicity), and ahara-asmayama (no restraint in appetite). Caraka prescribes in its texts exercise use to avoid obesity such as an hour-long walk should be taken every day once in the morning, and once in the evening. Younger people should be involved in playing rigorous sports and exercises. Hatha (sun- moon) yoga should be practiced regularly. Yoga with physical exercise increases the intake of Vayu which decreases Agni in the abdomen. In yoga, pranayama exercises are considered to be the basis of all breathing and air intake. Pranayama involves breathing in the air through the nostrils until the abdomen is filled and bloated with air. Once the abdomen if filled with Vayu, the air is forcefully and rapidly released through the nostrils. Practicing pranayama breaths continuously for as long as can be done depending on the ones practice in the breathing exercises, increases the intake of Vayu to diminish Agni in the abdomen. Caraka also prescribes the importance of oil massages. Since adipose has Kapha characteristics of oozing and foul smell, oil massages such as coconut or castor oil, can absorb intensify the bodily sweating leading to decrease in adipose tissues [14]. The following is a list of practices prescribed the Caraka verses to reduce obesity and maintain hormonal stress in order to prevent obesity (Caraka Samhita): sleeping properly at night, and avoiding day time sleeping, cleaning the body regular through bathing, oil massages to intensify sweating, regular practice of yoga, being involved in playing rigorous sports and exercises, walking for 2 hours everyday consumption of bitter or astringent foods, decrease or avoiding consumption of sweet or oily or overstored food. Maintaining healthy relationships with parents, sibling, children, spouse, friends, and extended family through communication as well avoiding over-stress worries and continuous self-education, having hobbies and work to increase mental activity are recommended. Other classical texts that contain information on obesity reduction therapies are Sushrat, Vagbhat, Madhavkar, and Ashtanga Hridya Sutra Shan. Ashtanga Hridya Sutra Shan contains information regarding the importance of bathing in warm water and massages to reduce obesity. It is recommended to consume fermented drinks made from barely (beer), honey, tubers, sugar cane and grapes (wine) as they come under the category of Vata by being bitter, astringent, and pungent in their tastes in order to increase Vayu in the body. Sushrat classical texts also emphasize the importance of oil massages and consumption of fermented honey to reduce adiposity [14]. Enema (basti) is another purification module to control Vata by clearing the bowls. Ayurveda prescribes natural healing for patients with digestive disorders, such as regularly and reasonably exercise and consume a reasonable and healthy diet. Ayurveda also stresses the importance of losing fat in gradual process and not by crash dieting to achieve the fat loss in a very short-term period [12]. Ayurveda promotes the use of caloric needs in diets. Ayurveda can prescribe multi-regiment or single plant, roots, and herbs for therapies. For obese patients in palliative care, dose of medication will be dependent on physical characteristics such as body mass index (BMI), age, and sex.

Bhavaprakash Niganthu traditional texts contain the collaboration of medications and therapies of

all other classical texts such as Caraka, Sushrat, and Vagbat. The Bhavaprakash text was written by Bhavamisra during the 16th century. This text compiles the information of 426 medications. Out of the 426 prescribed natural medications there are 54 herbs, roots, spices, and multi-regiment preparations that can be used to cure obesity and prevent non-alcoholic fatty liver disease (NAFLD) [15].

The natural medications used to reduce the fat and obesity came under six different categories known as: 1- kapha medo hara (reduce kapha and adipose tissue), 2-medo nashaka (destroying adipose tissue), 3-sthoulya nashaka (preventing obesity), 4-karashyakara (weight loss), 5-medorogahara (anti-obesity), and 6-lekhana (scarping). Arun and Manjunath established the activity of plants describing the mechanism by which these plants reduce obesity.

In the category of plants that may reduce adipose tissue (kapha medo hara): *Acaranthus aspera, Artocarpus heterophylum, Ceiba pentandra*, *Dolichos biflorus*, *Euporbia niriifolia*, *Erythrina indica*, *Fegonia cretica, Moringa oleifence*, *Ougeinia dalbergioldes*, *Phaseolus mungo*, *Piper longum, Schrebera swieteniodes, Solanum xanthocarpum, Spiranthus indica,* as well as a combination of *Ficus bengalensis, F. religiosa, F. racemose , F. lacar, and Thespesia populnea*. In the category of plants that destroy the adipose tissue (medo nashaka) are cited: *Acacia catechu*, *Butea utilis*, *Hordeum vulgare*, *Hydnocarpus* sp., *Setaria italic* and a variety of Choraka. A mixture of *P. nigram, P. longum, and Zingiber officinale* are recommended to prevent obesity (sthaulya-nashaka). *Coriander sativa* and *Coix lachymajobi*- are used for karashyakara (weight loss). *Dalbergia sisso* and *Terminalia arjun*a are recommended as anti-obesity (medorogahara) remedies. In the category - lekhana (scarping) the following plants are used: *Cinnamomum camphora*, *Commiphora mukul, Randia dumetorum* and the combination of *Ficus bengalensis, F. religiosa, F. racemosa, F. lacar, Thespesia populnea*, *Feronia limonia.* Also inferior grains and powder and oil of sesumum are used for the same purposes [15]. Information in Ayurvedic Classical text is written in the form of versus. This research article is going to investigate the roots, herbs, spices, plants, animal products, and therapies recommended by Ayurveda classical texts regarding obesity, NAFLD, and non-alcoholic steatohepatitis (NASH) through clinical studies.

The natural products belong to vata categories as they are bitter, astringent, and pungent and reduce kapha and Agni while increasing Vayu. Ayurveda also mentions any herb, root, spice, and plant can be used to cure a patient from an illness. Thus, to cure diseases such as obesity, NAFLD, and NASH the natural product has to be vata. Ayurveda prescribes the use of spices and herbs to reduce obesity. The Ayurveda spices can be incorporated in meals and beverages or can be eaten as is certain quantities every day to aid with metabolism, digestion, fat reduction.

Spices and herbs under vata category are used in Ayurveda for increase in metabolism and reduction in fat therapies include saffron, cumin, turmeric, cayenne pepper, fennel seeds, ginger, black pepper, and cinnamon. These spices are commonly used in meals, teas, and desserts. Each of these spices contains chemical compositions that are useful when it comes to reducing fat storage in the body. In South Asian cuisine, at least one of these spices is used in all meals.

Saffron is a spice originating from the pistols of saffron flowers. Saffron is mostly grown in Kashmir, Spain, and Italy. In many cuisines saffron is used to flavor rice and desserts. Saffron is a very popular spice in India and is used in Ayurvedic medications as a spice that can aid in digestion and reduction of fat cells in the body. The saffron contains following compounds: crocetin, safranal, crocin, and

picrocrocrin. Crocrin is responsible for the orange gold colour of saffron. Crocrin exhibits many pharmaceutical activities such as reducing cholesterol, triglycerides, and blood glucose (Table 1). Mashmoul and his colleagues [16] found that Wister rats injected with crocin developed a reduction in low density lipoprotein (LDL) and very low density lipoprotein (VLDL), cholesterol and triglycerides. The same team administered to diabetic rats safranal (80-240 mg/kg/day) along with crocin (50-150 mg/kg/day). This therapy decreased blood glucose levels and increased insulin levels [16] (Table 2).

Saffron-ethanol was capsulated and administered to 60 overweight women at a dose of 176.5 mg/day [16] (Table 1). After two months on the capsule, all women reported a decrease on unnecessary snacking appetite and loss of weight. Saffron is thought to aid in decreasing of fat because of the content of crocin. Crocrin is a natural pancreatic lipase inhibitor. Crocrin reduces fat absorption at a rate of 12% with a dose of 102 micro grams/Kg. Crocrin dysregulates mRNA expression of tumor necrosis factor (TNF)-alpha, adiponectin and leptin. Ethanol extract from saffron is highly recommended for appetite control [16].

Cumin is used to spice curries and also in some teas in South Asia, Middle East, East Asia, and North Africa. Cumin is recommended in Ayurveda as one of the effective spices in reducing obesity. Lime is recommended in decrease of lipid content in body in Ayurvedic texts. One randomized double-blind placebo-controlled clinical trial on the effect of *Cumin cyminum* L. plus Lime administration to observe weight loss and metabolic status in overweight subjects found that *C. cyminum* administered with lime may reduce body weight. C. cyminum inhibits serotonin re-uptake and increases levels of serotonin in synaptic clefts [17]. Limonene found in lime can reduce lipids by increasing lipolysis by histaminergic response and reduced appetite. Limonene is also anti-inflammatory and is found to improve insulin function [17]. To study the effectiveness of cumin with lime uptake, an 8-week clinical trial was conducted on 72 obese Iranian patients aged 18-50 years old (Table 1). Six of the patients were male, while 66 of the patients were female. The patients were divided in to three groups (placebo, low dose *C. cyminum* and lime intake, and high dose *C. cyminum* and lime intake). The average BMI in all three groups ranged from 31.1-33.2 kg/m^2. The patients in all three groups received a diet of approximately 2500 calories per day. The amount of carbohydrates, protein, and lipids received in the meals were also recorded. The study found that high dose intake of *C. cyminum* and lime resulted in significant weight loss compared to low dose treatment. On an average high dose intake patients lost 2.1 +- 1.7 kg, compared to low dose intake patients losing 1.2 +-1.5 kg, while placebo lost only 0.2 +-1.3 Kg. The patients also benefited from a reduction in plasma glucose levels, improved insulin sensitivity. BMI reduction in high dose intake was by 0.8 kg/m^2, while low dose intake was 0.5 kg/m^2, and placebo only 0.1 kg/m^2. The study concluded that high dose intake of *C. cyminum* with lime is beneficial for weight loss and obesity treatments [17].

Turmeric (*Curcuma longa*) is a spice used in various cuisines around the world. Curcumin is the principle ingredient used in alternative medicine for its anti-cancerigenic properties being effective in melanoma, brest, lung and pancreatic cancer [18, 19]. It has antiseptic and anti-inflammatory properties. Turmeric with boiling milk drank during cold can relieve sore throat and used as a cream rubbed on wounds and pimples to provide protection against bacteria.

Table 1 Ayurvedic medicines used to treat obesity, NAFLD, NASH, and cirrhosis

Author	Ayurvedic plants and medicine	Clinical setting	Parameter measured	Results
Mashmoul *et al*., 2013 [16]	Saffron-ethanol, 176.5 mg/day.	60 over-weight women	Cholesterol triglyceride glucose, BMI	Loss of appetite, reduction of BMI- body mass index
Taghizadeh *et al*,.2016 [17]	Cumin with Lime *(Cumin cyminum*)	Obese 66 female, 6 male; aged 18-50; Dose: high 0.8 kg/m^2, low- 0.5 kg/m^2, placebo 0.1 kg/m^2 ; 8-weeks	BMI	Significant weight loss for high dose patients, weight loss occurred in all groups.
Janssens et al., 2013 [20]	Cayenne pepper (capsaicin)	9 male, 10 female (age 18-50), 2.56 mg red chili pepper (capsaic)	Blood pressure, BMI, substrate oxidation, body composition	Capsaicin reduced the effects of negative energy balance; no increase in blood pressure.
Ofner et al., 2013 [21]	*Salica reticulate* (glucosidase inhibitors)	40 individuals aged 30-60; 200 mg *S. reticulate*, Vitamin D_3 1.6 µg (i. e. 64 IU) x 3 times/4 weeks	BMI	BMI, reduction on an average of 1.8 Kg and 5.3 Kg
Bhagiya et al., 2015 [22]	Lekhana Basti (medicated enema)	2 groups: 15 obese age 16-60 years Group A - Lekhana Basti; Group B processed drugs	Body fat reduction	Group A lower obesity compared to group B. Group A 13.33% - completely cured, none group B
Rioux et al., 2014 [23]	Ayurvedic Yoga Therapies	22 adults:17 initiated, 12 completed 3-month intervention	BMI	Mean weight loss at 3 months 3.54 kg (SD 4.76); 6 months: 4.63 kg, (SD 6.23) and 9 months: 5.9 kg (SD 8.52)
Patel et al., 2015 [24]	*Piper longum, P. purpurea*, *E. alba*, *Boerhavia diffusa, T., Berberis aristata DC, Cyperus rotundus L. Curcuma longa L, Azadirachta indica, Tinospora cordifolia*, *Zingiber officinale*, *Picrorhiza kurroa*; *Tephrosia purpurea*, *Phyllanthus niruri* Sensu Hook. F., NH4Cl, KNO3, KAl(SO4)	68 cirrhosis patients 48 male; 20 female. Duration 24 weeks Medium age 46.65 years; 26 alcoholic cirrhosis; 12 dropped out. Doses of *P. longum* from 1 g/day to 5 g/day; decoction 10□g/40mL/ day; powder 5.5 grams/day	Oedema loss of appetite, general weakness, nausea vomiting, abdominal girth, urine output, albumin, bilirubin, Child-Pugh score.	Serum bilirubin increased from 3.74 ± 4.59 to 6.5 ± 4.04 % in seven weeks, serum albumin increased. The Child-Pugh scores after treatment: 50 patients in Group A, 6 patients in Group B, none Group C.

Table 2 Experimental studies *in vivo* and *in vitro*

Author, Year	Ayurveda (Constituents)	Animal	Parameter	Results
Mashmoul *et al*., 2013 [16]	Saffron (crocetin safranal, crocin, and picrocrocrin)	Wister rats 10 days receiving crocetin 25-100 mg/kg/day	Cholesterol, triglycerides, glucose	Reduction in LDL, VLDL cholesterol, triglycerides, glucose, Insulin increased.
Shah et al., 2011 [25]	Black pepper (1-piperoyl piperidine (40 mg / kg) + sibutramine (5 mg / kg)	Male Sprague-Dawley rats weighing 400 – 450 g fed for 11 weeks	Blood samples, fat pad analysis, serum triglyceride, total cholesterol, LDL, VLDL , HDL levels	Piperine reduced triglyceride, total cholesterol, LDL, VLDL, HDL. Thyrogenic activity, dyslipidemia.
Camacho et al., 2015 [26]	Cinnamon (cinnamaldehyde)	Mice treated 5 weeks 250 mg/kg/day	BMI	Fat mass before the study was 5.2 g+-0.3, after 4.5g
Winarsi, 2014 [27]	Cardamom (ethanolic cardamom leaves extract-ECLE)	45 rats divided into 3 groups, 1- diabetic rats fed ECLE, 2-diabetic rats no ECLE, 3- non-diabetic rats no ECLE 14 days.	Glucose, cholesterol, BMI	ECLE reduced blood glucose of ECLC-diabetic rats from 201.7 to 102. 8 mg/dl (P = 0.017), cholesterol from 77.6 to 56 mg/dl (P = 0.025)
	Six plants containing pancreatic lipase (PL) inhibition potential	*In-Vitro* assays in adipocytes	Lipid accumulation, adipocytes	Oroxylin A, chrysin + baicalein inhibited lipid accumulation (75.00±5.76%, 70.21±4.23%;77.21±5.49%; in control 50μM) and PL enzyme (69.86±2.96%, 52.08±2.14%; 45.06±2.42% PL inhibition 250μg/mL)
Jadeja, 2014 [28]	*Picrorhiza kurroa*	Rats (200-400 mg) 4 weeks	Lipid accumulation	Significant decrease in lipid accumulation

ECLE-ethanolic cardamom leaves extract, HDL-High density lipoprotein, LDL-Low density lipoprotein, PL-pancreatic lipase, VLDL-Very low density lipoprotein.

Turmeric is used in beauty products, as it is a natural anti-bacterial promoting healthy and glowing skin. Belcaro et al. [29] studied its use as anti-inflammatory agent in osteoarthritis. Apart from being an anti-inflammatory, Ayurveda recommends that turmeric also can be used to reduce fat in obese

patients. Turmeric contains 2-8% curcumin [30]. It is safe for most patients. However, high doses and long term use can cause nausea, diarrhea and indigestion as well as worsening of gallbladder disease [29].

Curcumin interacts with white adipose tissues and reduces inflammation. TNF-α and monocyte chemoattractant protein-1(MCP)-1 expressions are reduced along with plasminogen activator inhibitor type 1(PAI-1). Adipocyte differentiation expression is reduced and promotion of antioxidant activates occur due to interactions of curcumin in turmeric [30]. Thus turmeric can reduce and prevent obesity and obesity related diseases. Turmeric can be added to meals of drank with milk.

Cayenne pepper is a popular spice used in Asian and African cuisines. Cayenne pepper is very spicy and highly prescribed by Ayurveda for weight loss and body lipid management. Cayenne pepper in South Asia is a common ingredient in curries and stews. The reason why cayenne is useful in weight loss and weight management is because of its main component, which is capsaicin. Capsaicin promotes lipid reduction through the process of thermogenesis and fat oxidation in the body. A clinical trial was conducted on 19 healthy Caucasian adults [20]. The mean BMI was 23.3±2.9 kg/m^2. The subjects were given a dose of 2.56 mg of capsaicin in form of red chili pepper. The study took 24 hours to conduct and information regarding blood pressure, BMI, substrate oxidation, and body composition was taken into account. Four of the patients however dropped out of the study for personal reasons. The study examined the 24-hour effect of capsaicin on energy expenditure, substrate oxidation, macronutrient balance. Long-term use of capsaicin at a dose of 135 mg/day led to an increase in oxidation and fat reduction [20].

Fennel seed diet is used as a spice coming from a flowering plant belonging to the carrot family. Fennel is referred to in Ayurveda as an appetite suppressant. Fennel seeds can be added to meals for flavour, or can be drank with tea. To reduce weight in obese patients, meal intake must be strictly regulated to a certain amount of energy that will promote weight loss. Chewing on fennel seeds can reduce appetite thus reducing the amount of food intake in obese patients. Chewing on fennel seeds releases serotonin and dopamine that act as appetite suppressants. When appetite is suppressed, unnecessary cravings are reduced resulting in reduction of food intake. By this method, fennel seeds can promote in weight loss for people who are overweight or obese.

Ginger is a spice and root that is widely used in many applications of Ayurveda and folk medicines around the world. Ayurveda recommends use of ginger for many purposes such as decreasing acidity, body lipid burning to promote weight loss, anti-motion and anti-nausea sensations, anti-septic properties for skin, and anti-ulcer stomach problems. Ginger is found in almost all cuisines worldwide. In South Asia, ginger is a basic ingredient for curries and can be drank in the form of tea. Many studies have been conducted on ginger when it comes to promoting weight loss and fighting against obesity. Ginger intake has been found to reduce cholesterol, triglycerides, phospholipids, and serum-lipoproteins in the body. This is due to the fact that ginger creates thermogenesis and boosts metabolism. Moreover, ginger absorbs acidity in the stomach [31].

Black pepper is used to flavour meals and is the most common spice grown through South Asia. Ayurveda prescribes the use of black pepper to increase body heat, relieve sore throat during colds due to antiseptic properties, and reduce obesity. Black pepper is shown to reduce obesity due to its main constituent of piperine (1-piperoyl piperidine). A decrease in adiposity can be achieved by an

increase in melanocortins (MC), MC-4, cleaved from pro-opio-melanocortin (POMC) [25]. MC-4 receptors help reduce appetite, increase energy expenditure and insulin sensitivity. Without MC-4, there would be no increase in leptin and / or insulin activity, which is dependent upon the peripheral leptin / insulin production, transport across the blood-brain barrier, and effect upon the central nervous system target receptors [25]. Piperine is a melanocortin agonist. An animal study involving Male Sprague-Dawley fat-fed rats was conducted to determine the effectiveness of piperine in fat reduction. For 11 week period and rats were treated with piperine (40 mg / kg) and sibutramine (5 mg / kg), respectively (Table 2). The study found that piperine significantly reduced serum triglyceride, total cholesterol, LDL, VLDL, HDL levels, which reduced dyslipidemia. Thyrogenic activity is possessed by piperine and shows great potential in management of dyslipidemia by dietary supplementation with nutrients [25].

Cinnamon is considered to be an exotic spice. Cinnamon is used for its flavour in rice dishes and in caffeine beverages. Apart from being an exotic bark spice filled with flavour, cinnamon contains Ayurveda described health benefit values including lipid management and weight loss. Cinnamon's main constituent, cinnamaldehyde, which is responsible for its flavour reduces food intake. The effects of cinnam-aldehyde (250 mg/kg/day) containing food were administered for 5 weeks to mice. Fat mass, lean mass, plasma glucose and insulin levels, cholesterol, triglycerides, adiponectin, and leptin were measured [26]. The average fat mass before the study was 5.2 g+-0.3, and after 5 weeks the fat mass reduction became 4.5g+-0.3 [26] (Table 2). The authors conclude that cinnam-aldehyde is a natural ghrelin suppressant, which can be used as an anti-glycemic drug and enhances insulin sensitivity. Apart from spices that are beneficial as therapies in cases of overweight subjects, Ayurveda recommends the use of roots, fruits, and plants.

Salacia sp. roots, *Aloe vera*, Amla, cardamom leaves, and many other herbs and roots can be cooked or used as ingredients in teas, but preferable eaten raw as cooking and heat can alter their nutrients. *Salacia reticulate* is one of the roots rich in alpha-glucosidase inhibitors. A study was conducted on 40 healthy participants aged 30-60 years that took combination 200 mg of *S. reticulate* and 1.6 µg (i.e. 64 IU) Vitamin D_3 3 times/day with the meals over a period of 4 weeks [21]. The study found that the BMI was reduced with two groups losing on an average of 1.8 Kg and 5.3 Kg [21]. The study concluded with promising results on *S. reticulate* and Vitamin D_3 for treatment of obesity. *S. reticulate* roots have also found to be consumed heavily in Japan and the United States as food supplements due recent pharmacological studies having demonstrated that *Salacia* roots modulate multiple targets: peroxisome proliferator-activated receptor-alpha-mediated lipogenic gene transcription, angiotensin II/angiotensin II type 1 receptor, alpha-glucosidase, aldose reductase and pancreatic lipase [21]. It is highly recommended for type 2 diabetic and obese patients to take as supplements.

Bio-assay of *Salacia* roots indicates mangiferin, salacinol, kotalanol and kotalagenin 16-acetate are partly responsible for these multi-target regulatory activities [21].

Aloe vera is a plant that is grown in tropical climates and is used for agricultural and medicinal purposes. It can be used in meals like other vegetables. *A. vera* leaves consist of a waxy gel that has cooling and antibacterial properties and can be used to clear acne, pimples, moisturize skin, relieve and provide antiseptic to wounds, and cool skin burn injuries. Ayurveda recommends *A. vera* for

reduction of fat as its plant cholesterol constituent phyto-sterols modulate glucose and lipid metabolism resulting in reduction of cholesterol levels and blood lipids. *A. vera* also modulates PPAR (peroxisome proliferator activated receptors), responsible for metabolism of carbohydrates and lipids, to increase its efficiency [32].

Amla, Indian gooseberry, is a fruit that is grown throughout India and is popularly consumed. It is a natural refresher and due to being rich in nutrients it has many pharmaceutical applications when it comes to anemia therapy, urinary problems treatment, hair growth therapy in form of oil, relieves headaches and can be used in obesity and weight reduction treatments as well. Amla can be consumed on a regular basis to increase metabolism. The herb is rich in chromium, zinc, and copper [33]. Amla is highly bitter and astringent in taste and comes under the category of Vata to reduce fat [34].

Cardamom leaves are aromatic, flavour rich and exotic spice leaves that add flavour and aroma to various sorts of dishes. Cardamom leaves could be a potential therapeutic for obesity as they promote weight loss. The anti-diabetic and hypo-cholesterolemic properties of ethanolic cardamom leaves extract (ECLE) was described in an animal study [27]. The experiment was conducted on 45 rats divided into three groups, first group consisting of diabetic rats fed with the extract, the second group of diabetic rats not given ECLE, and third group of non-diabetic rats not given the extract. The study was conducted over a period of 14 days. The blood glucose level of rats group I decreased from 201.7 to 102. 8 mg/dl (P = 0.017), cholesterol level from 77.6 to 56 mg/dl (P = 0.025) in first group of diabetic rats [27] (Table 2).

Ayurvedic medicinal plants contain anti-adipogenic and pancreatic lipase inhibitors potential [35]. *In vitro* anti-adipogenic assay using 3T3-L1 preadipocytes and pancreatic lipase inhibition assay concluded that *Oroxylum indicum* barks were most effective in lipid accumulations and in enhancing pancreatic lipases inhibition. *In vitro* assays showed an anti-adipogenic effect (59.12±1.66% lipid accumulation as compared to control at 50 µg/mL dose) and pancreatic lipases inhibition 89.12±6.87% at 250µg/mL dose). It was found that oroxylum A, chrysin, and baicalein inhibited lipid accumulation in 3T3-L1 preadipocytes (75.00±5.76%, 70.21±4.23% and 77.21±5.49% lipid accumulation respectively in comparison to control at 50µM dose). Pancreatic lipase inhibition was 69.86±2.96%, 52.08±2.14% and 45.06±2.42% at 250µg/mL dose [35]. PPARγ and C/EBPα, major adipogenic transcription factors, were also inhibited by oroxylum A and chrysin. The authors concluded that the substances found in the Ayurveda plants have potential to anti-obesity effects [35].

In Ayurveda texts medohara means anti-obesity and lekhaniya dravyas means hypo-lipidemic. These are two categories of drugs. Abinaya and Pavitra [36] in their work entitled “Management of obesity and its related disease by herbal medicines” investigated these two categories of Ayurveda drugs by compilation and tabulating the scrapes of useful parts of the herbs. There were over 160 different formulations in the form of roots, dried fruits, and barks. Information from classical literature was taken into account and included in the tabulation [36]. The drugs were judged on their taste, quality, potency, and metabolism. The study concluded that Medohara and Lekhaniya Dravyas consisted of multi-pharmalogical properties that confirmed both hypolipidimic and hypoglycemic activities [36].

Ayurveda contains information in its classical texts about other naturally found ingredients like honey, which can be used to promote fat reduction. It is recommended that honey be used to sweeten beverages or desserts than sugar.

When it comes to sweetening meals and beverages, smaller amount of honey can be used than sugar to achieve the same amount of sweetness but for far lesser calories. Fewer calorie intake, results in greater amount of weight loss. Sushrat recommends drinking fermented honey known as "honey wine", which is bitter and astringent in taste as it increases Vayu to decrease Agni [34]. Ayurveda also contains information regarding procedures such as enema to reduce fat. One study conducted by Bhagiya et al. [22] "Comparative clinical study of lekhana basti and shaman sneha (Triphaladi Taila) in the Management of Sthaulya (Obesity)" found that Ayurveda's lekhana basti (medicated enema) was far more effective than shaman sneha (processed drugs). Two groups consisting of 15 obese Indian patients each with an age range of 16-60 years were examined. Group A was given treatment through Ayurveda's Lekhana Basti while Group B was given treatment by Shaman Sneha. It was found that Group A exhibited far greater results in obesity treatment than compared to group B. For group A 13.33% of patients were completely cured, while none for group B, 46.67% of patients got moderate results from group A, while group B got 73.33% moderate results from patients). In group B, 26.67% of patients got mild results. All patients experienced some improvement [22]. It proved Ayurveda's treatment using Ayurveda's Lekhana Basti (medicated enema) was far more effective than Shaman Sneha (processed drugs) as Lekhana Basti contains hypolipidimic properties) [22]. Ayurveda classical texts emphasize that it is not just what you can eat in terms of spices, herbs, plants, roots, and other natural ingredients to prevent or reduce obesity, but it is also about what you eat on a daily basis and your everyday lifestyle that plays an important role when it comes to preventing and reducing obesity. Every country provides health guidelines, for example a food pyramid, to its citizens on calorie intake and food intake based on each food group such as grains, fruits and vegetables, meat and protein, dairy products, oils and fats, and sweets. These guidelines are dependent on age as well. Ayurveda provides guidelines by dividing food into categories, timing to consume meals and yoga and physical activity practices, which should be followed by everyone especially people seeking weight management and battling obesity. According to Ayurvedic science, weight gain is cyclic and is dependent on the season. Ayurveda categorizes food into three different categories: rajasic, tamasic, and sattvic.

Rajasic food stimulates the body and is neither beneficial nor harmful. Spicy, salty foods, caffeinated drinks, chocolate, alcohol, eggs, and cola are examples of Rajasic food.

Tamasic foods are considered detrimental to health if consumed on a regular basis. Tamasic foods include processed meats, canned vegetables, frozen meals, cheese, or any vegetable or meat that has been kept overnight in the refrigerator.

Sattvic foods are considered the healthiest among the food groups that help to maintain a clear body and mind. Examples of sattvic foods are fresh vegetables, fruits, beans, legumes, and any organically grown product consumed within day.

Ayurveda recommends avoiding Tamasic .

Sattvic foods are recommended for regular consumption. Ayurveda gives importance to eating seasonal. Animals, including humans, must practice a cyclic diet. During winter, the body goes into

hibernation mode. Tendency to eat during colder seasons increases and the body will require foods rich in nutrients proteins, and lipids to keep warm. During spring, the body comes out of winter hibernation mode and will require low calorie diets such as leafy greens and fibrous fruits such as apples and pears as the body will need to shed extra mass gained during winter season [34]. During summer months, when temperatures are high, body will require carbohydrate rich foods such as vegetables, potatoes, rice, bread, and fruits as heat can cause sweating and body will more sugar to remain active.

When it comes to quantity of food that must be consumed, Ayurveda's formula is 1/3 solid food, 1/3 water, and 1/3 air in stomach after consumption [34]. One must not over eat, and must keep 1/3 of stomach empty for ease in digestion. For food consumed, equal volume of water must be consumed as well. A technique to measure food and water intake is by literally dividing your abdomen into three equal parts for food, water, and air. Water is essential to reducing obesity or maintaining healthy weight as it help clear out any lipid molecules in the digestive system by circulating through it and the entire body. Water is a natural purifier.

A way to prevent oneself from over-eating is to practice breathing exercises known as Pranayama and yoga poses. If breathing during Pranayama and yoga poses is performed properly, than this activity brings mental balance [12] through increasing Vayu and decreasing Agni. With clear mind, healthy decision making process takes place and mindful eating and interest in being physically active to keep healthy occurs.

Weight loss therapies have been used to determine whether Ayurveda practices are beneficial. A study was conducted in Tuscan Arizona consisting of twenty-two voluntarily participating adults of whom 17 initiated the intervention, and 12 completed the 3-month intervention [23]. The self-reported program found that the mean weight loss at 3 months was 3.54 kg (Standard Deviation-SD 4.76); 6 months: 4.63 kg, (SD 6.23) and 9 months: 5.9 kg (SD 8.52) with 90% of the participants found to be satisfied undergoing Ayurveda yoga weight loss therapy intervention [23].

Severe obesity and insulin resistance can lead to NAFLD and NASH. In order to prevent NAFLD from occurring in the first place, obesity must be reduced through diet and exercise. Modern studies are currently being conducted for use of Ayurveda medications in direct treatment of NAFLD and NASH. There are Ayurveda plants that are currently potential for direct treatment of NAFLD and NASH.

A perennial herb, *Picrorhiza kurroa* found in the Himalayan region is prescribed by Ayurveda for chronic diarrhea, scorpion stings, and liver inflammation. This herb contains a rhizome that can reduce liver inflammation, insulin resistance, and hepatic lipid accumulation [28].

One study investigated rats that were given a dose of 200-400 mg of *Picrorhiza kurroa.* There was a decrease of lipid accumulation significantly after 4 weeks. The mechanism of the *P. kurroa* ribosome still needs to be determined [28]. Another similar perennial herb is *Platycodon grandiflorum*, as it provides cure for the same illnesses ad *P. kurr*oa and has similar effects on reduction and regulation of NAFLD and NASH treatment in rats [28].

Pomegranate fruit is an ideal candidate for NAFLD induced by insulin resistance. This is due to pomegranate's constituent PPAR α/γ which can be used in insulin resistance therapy and increase in hepatic gene expressions of PPAR-α, CPT-1, acyl-CoA oxidase (ACO), and reduced SCD-1 [28].

Coriandrum sativum L, coriander is known in the Mediterranean region, Africa and the Middle East,

central Asia, India and China. *C. sativum*, an aromatic annual plant, is well known for its use in jaundice. Essential oil, flavonoids, fatty acids, and sterols have been isolated from different parts of *C. sativum*. The plant has a very effective antioxidant profile showing 2, 2-diphenyl-1-picrylhydrazyl radical scavenging activity, lipoxygenase inhibition, and phospholipid peroxidation inhibition, iron chelating activity, and anti-lipid peroxidation due to its high total phenolic content with the presence of constituents like pyrogallol, caffeine acid, and glycitin. The extract of the plant was shown to be hepatoprotective in an animal model of carbon tetrachloride-induced liver injury [37]. Coriander is also able to significantly decrease liver fat accumulation and increases in beta-hydroxyl, beta-methyl glutaryl CoA reductase and plasma lecithin cholesterol acyl transferase activity. Coriander being an excellent antibacterial and antifungal, effective against *Eshcheria coli, Salmonella sp. and Candida albicans* [38].

Coriander seeds showed a significant hypolipidemic action in rats given high fed diet with cholesterol. The levels of total cholesterol and triglycerides decreased significantly in the tissues of the animals of the experimental group which received coriander seeds. Significant increases in beta-hydroxyl, beta-methyl glutaryl CoA reductase and plasma lecithin cholesterol acyl transferase activities were noted in the experimental group.

Low density lipoprotein (LDL), and very low density lipoprotein (VLDL) decreased while high density lipoprotein (HDL) cholesterol increased, in the experimental group compared to the control group. An enhanced hepatic bile acid synthesis and the increased degradation of cholesterol to fecal bile acids and neutral sterols appeared to account for the effect hypocholesterolemia produced by *Coriander sp* [39]. More research currently needs to be conducted on these fruits [40].

NASH could lead to liver cirrhosis which represents one of the top causes for deaths worldwide. A clinical trial on Ayurvedic, medication using multi-regiments in treatment of liver cirrhosis was conducted. The clinical trial consisted of 68 cirrhosis patients of which 48 were male and 20 were female [24]. The mean age was 46.65 years and 26 of the patients had developed cirrhosis due to alcohol abuse [24]. Twelve patients dropped out of the study due to personal issues not regarding the study. The study took place over 24 weeks.

The *Piper longum* was given twice daily from 1 gram to increase of gram per day until 5 grams a day [24]. Five grams a day was given for 5 days, and the dose of *P. longum* decreased to 1 gram a day by 1 gram each day. A compound decoction, compound powder, and whole plant were administered containing multi-regiment Ayurvedic medicines (Table 1).

Ingredients in the compound decoction and powder were *Boerhavia diffusa* L. (anti-inflammatory, hepatoprotective, and antioxidant effects), *T. purpurea*, and *E. alba*, were administered since experimental studies suggest a hepatoprotective, and *P. kurr*oa which has been shown to have liver protective and anti-inflammatory activities [24]. Compound decoction at a dose of 10 g/40mL/day and powder at a dose of 5.5 grams/day were administered. Clinical features observed were oedema, loss of appetite, general weakness, nausea and vomiting, abdominal girth, and urine output. The reduction in severity of complaints was graded from 0 to 3, with 0 being the best grade and 3 being the worst grade to receive in these categories. Albumin and bilirubin secretions were also considered parameters, along with Child-Pugh scores [24].

After the Ayurveda therapy was administered to the patients, there were significantly improved results as oedema was reduced by 83.9%, appetite increased by 64.7%, general weakness declined by 54.7%, nausea and vomiting were relieved by 90.9%, abdominal girth decreased by 19.7% and urine output increased by 266.3% (Table 1). In conclusion, Ayurveda has significantly positive effect on patients with liver cirrhosis [24].

Cannabis sp. has a special place in Ayurveda. Ayurveda recommends consumption of cannabis, known as ganja, for treating diseases. Abusing the consumption of the plant through recreational purpose is considered sinful. *Cannabis* should be purified before consumption through swedana, a steam treatment, for 3 hours and then must be washed, dried, and roasted with ghee according to Dola Yantra [41]. *Cannabis* has been consumed for thousands of years in the form of a drink known as bhang. Bhang is cannabis leaves boiled with milk and spices such as cumin, saffron, cardamom, turmeric, and garam masala. Variations of bhang depend on the spices that have been used. Bhang is considered a sacred drink as according to Hindu mythology. Cannabis leaves can also be found in pickles, food products and medication formulations.

Caraka Samhita, Sushrat Samhita, Ananda Kanda, and Shargandhara Samhita are the classical Ayurvedic texts that contain information regarding cannabis. Under the classifications of kapha, vata, and pitta, cannabis comes under pitta due to the fact that it is dry, hot, astringent, pungent, dulling, and neurotic [12]. Pitta is responsible for digestion, cravings, and hunger and aggravates the cosmic fire Agni within oneself.

Due to the fact Cannabis consumption increases Agni, therefore aids in short-term digestion, but will cause cravings and thus increase consumption that will lead to weight gain, Cannabis does not aid in preventing or curing obesity. Cannabis being astringent and dry will lead to dehydration. It can diminish energy levels, and no longer be effective if over-used.

Many studies have been performed to determine whether or not Cannabis can be used for the treatment of obesity. Investigation of different community samples concluded that Cannabis aided in weight gain in underweight patients with cancer and Human Immunodeficiency Virus-(HIV) infected individuals. However, normal BMI and obese individuals, slowly and gradually gain weight [42]. Cannabis can be used for the treatment of nausea. Long-term use of Cannabis can lead to constipation [41]. Cannabis specifically is known to treat irritable bowel disease, and chronic malabsorption. Cannabis also comes under the category of having tamasic properties as it is naturally sedative towards the body and mind, thus it can help in relieve of physical pain with patients undergoing chemotherapy or other physically debilitating treatments [41].

As mentioned, Cannabis should be used for healing purposes. *Cannabis* should be taken in with anupanas (used to direct and enhance properties of herbs) such as milk, sugar, honey, and ghee. The prescribed dosage of *Cannabis* should be 250-500 mg, 1-3 times a day. Apart from bhang, other formulations that can be used to consume cannabis are Jatiphaladi Churna, Kumari Asav, and Madan Modaka [41].

Although Ayurveda vata natural products are a promising solution in the battle of obesity, NALFD, cirrhosis, it comes with its concerns. Many studies are currently being conducted on the safety in use of Ayurveda products.

Some Ayurveda products are contaminated with toxic heavy metals, particularly lead, due to variety of reasons including poor manufacturing practices of the medications [1][43].

One case study was conducted to determine whether or not the used of Ayurveda medicine had been associated with heavy metal poisoning, particularly lead. One case found that a 65 year old Asian man had been ingesting 10 different Ayurveda pills for his diabetes [44]. His blood level concentration of lead was 6.58 micro mol/l, and after undergoing treatment declined to 1.11 micro mol/l [44]. A 59 year old Indian man had been taking Ayurveda medicine for his diabetes, his initial blood lead level concentration was 4.1 micro mol/l, after treatment that required him to stop Ayurveda medicine, his blood lead level fell to 3.5 micro mol/L [44]. A 26 year old Asian man was taking Ayurveda medications for his anemia, his blood lead level was 3.85 micro mol/L, after treatment without Ayurveda it fell to 1.07 micro mol/l [44]. A 57 year-old female patient had been using Ayurveda for her diabetes and her blood lead level was 5.9 micro mol/L, after undergoing treatment without Ayurveda it fell to 1.2 micro mol/L. A similar case was found for a 59 year-old man [44]. This study found potential lead toxicity in Ayurveda at a dangerous level. Ayurveda medication is also recommended for diabetic patients in India [44].

Ayurveda is becoming a common source of medication in all parts of the Western world. In United States, complementary and alternative medicine, or integrative medicine is used by 33.2% of the population [45]. Nahin and colleagues [46] reported that the cost of complementary and alternative medicineis high. . Ayurvedic medicine is part of the alternative medical systems [47]. The potential usefulness of integrative medicine including Ayurvedic medicine for some patients should be taken in consideration. However it is a need for the clinician to be aware of what the particular patient is using and the potential interactions with the therapeutics. Moreover, the patient and the clinician should take in consideration that the integrative medication might contain excess amounts of heavy metals.

In United States, heavy metal screening was performed in 115 users of Ayurvedic medications [48]. Elevated levels of lead were present in 46 of 115 users (10 μg/dl or above) [48] Dangerous concentrations of lead can lead to various adverse health effects. For example, a 69 year-old Caucasian male suffering from depression, fatigue, generalized weakness, constipation, anorexia, and weight loss was found to have elevated levels of lead following regular consumption of Ayurveda medications [49]. A 58-year-old woman was suffering from abdominal pain, anemia, liver function abnormalities, and an elevated blood lead level was found to have been taking the Ayurvedic medicine Jambrulin [50]. Lead poisoning leads to various symptoms ranging from mild anemia to encephalopathy [51].

There have been even cases of extreme lead poisoning from use of Ayurveda medications. A 29-year-old Indian suffered from abdominal pain, nausea, constipation, and fatigue for 2 weeks [52]. He had been taking Ayurveda medicine as pain control at a dose of approximately 15 g/day. His blood samples contained a high lead concentration of 36,000 mcg/g, which is over 25,000 times the maximum daily acceptable dose [52]. Although 95 % of lead poisoning cases in United States are due to occupational exposure, 5 % of the cases are from use of herbal and traditional medicines [52]. During 2000-2003, a total of 12 cases of lead poisoning among adults in five states associated with Ayurvedic medications or remedies were reported to the CDC [53].

It has also been recommended that young children should not receive any herbal and traditional medications, since all may have f some degree of toxicity. A 9-year-old Indian boy in Florida died from lead toxicity found in herbal medications taken for common cold. Extremely high concentrations of lead were found in the boy's blood, spleen, kidney, and intestines [43].

Along with lead, Ayurveda could contain arsenic, mercury, and other toxic heavy metals. Tests were conducted on Ayurvedic medications from South Asian grocers in the Boston area. Concentrations (μg/g) of lead, mercury, and arsenic in each HMP were measured by x-ray fluorescence spectroscopy. The study concluded that 1 in 5 medications contained potentially harmful levels of lead, mercury, and/or arsenic [54]. Fourteen of 70 HMPs contained heavy metals: lead (n = 13; median concentration, 40 micro/g; range, 5-37,000), mercury (n = 6; median concentration, 20,225 micro/g; range, 28-104,000), and/or arsenic (n = 6; median concentration, 430 micro/g; range, 37-8130) [54]. Another similar study conducted in India found that six samples of medicines had an arsenic concentration of 36-8130 milligrams/grams, which is considered highly unsafe. Dangerously high levels of cadmium were also found at 16.438-29.796 milligrams/grams [55]. These toxic metals could expose patients to other adverse health problems in these concentrations. During 2015, Wisconsin Division of Public Health reported a 64 year old female patient suffering with anemia and fatigue and had been taking herbal medications had high levels of arsenic and lead in her urine samples [56]. Despite reports of Ayurveda containing dangerous levels of toxic metals, there are these who believe that Ayurveda medications do not contain any heavy metal toxins. They claim that Ayurveda is pure due to multiple cycles of incineration required for manufacturing processes [56]. Solid evidence does not back up their claims.

The reason for high levels of heavy metals in toxicity in Ayurveda is due either to the heavy metals naturally being found in the roots, barks, and fruits, or poor manufacturing practices and adulteration. Studies have found that Ayurveda medicine manufactured by different countries have different levels of toxicity claiming that some developing countries need to improve their manufacturing practices compared to industrialized nations [1].

A study was conducted using three variants A, B, C of Ayurveda medicine, it was found that cadmium content of two variants A and C was within permissible limits whereas cadmium content of variant B was 2.98 ppm about ten times higher than the permissible. The study concluded that toxicity on Ayurveda depends on where and how it is manufactured [57]. A Pakistani study found that of 22 Ayurvedic HMPs purchased, 41% contained arsenic and 74% contain mercury and lead in Pakistan, while in England 30% of Ayurveda medicine contained toxic metals [58].

Another major reason for toxic elements in products apart from manufacturing issues is the use of pesticides on fruits, barks and roots. Various herbal roots were investigated in the Himalayan Region and were found to have concentrations of toxic metals arsenic, cadmium, zinc, and lead in (0.2-8.34 mg/kg arsenic, 0.11-0.48 mg/kg cadmium, 2.5-6.0 mg/kg plumb, 7-32 mg/kg zinc) [59]. WHO also collected data from residual pesticides on Ayurveda Dashmoola (Ten Roots). Toxic metals arsenic, cadmium, zinc, and lead were found [1]. Organic chlorine residue concentrations were present in the roots. Lead and cadmium concentrations were far above the WHO safety guidelines [1]. Sometimes the manufacturing practices of a country or use pesticides may not be the only reasons for such concentrations of toxic metals. Interestingly there is one branch of Ayurveda medicine called Rasa

Shastra, which combines minerals, metals, and gems in its medication [60]. During August-October 2005, 230 Rasa Shastra medications were brought online from United States and Indian manufacturers [60]. Although manufacturers from both countries claimed safe and excellent quality manufacturing practices, the prevalence of metals in US-manufactured products was 21.7% (95% CI, 14.6%-30.4%) , and 19.5% (95% CI, 11.3%-30.1%) in Indian products (P =0.86) [60]. Lead, mercury, and arsenic were present in one-fifth of both US-manufactured and Indian-manufactured Ayurvedic medicines brought online [60].

Ayurvedic heavy metal toxicity is not the only concern, all herbal medicines including Ayurvedic medicines have pyrrolizidine alkaloids. Pyrrolizidine alkaloids are naturally produced by plants as self defense mechanisms. These alkaloids are highly toxic to the liver and may cause liver damage, veno-occlusive disease of the liver [4]. Herbal medications containing comfrey have even been banned in countries like Germany and Canada after epidemics in Jamaica, India, and Afghanistan due to veno-occlusive disease leading to cirrhosis and eventually liver failure. These cases were a result of pyrrolizidine alkaloids found in comfrey leaves [60, 61]. In North Western India herb *Heliotropium eichwaldii* taken by patients contained pyrrolizidine alkaloid, heliotrine. From regular intake of this herb, two of the patients developed fulminant hepatic failure, four patients developed decompensated cirrhosis [62]. These were considered chronic and acute liver failures. Herbal supplements contain the most dangerous pyrrolizidine alkaloids such as kava, chaparral and germander can account for half of all liver failures [63].

Other herbal products from plants such as honey used as natural medicine for weight loss, purifying blood, moisturizing skin, and other medical purpose also contain amounts of pyrrolizidine alkaloids [61]. Due to this concern, honey is internationally regulated as it may come from pyrrolizidine alkaloid rich plants. Pyrrolizidine alkaloids can also make their way into the food chain from honey, milk, and vegetables used as herbal medicines or part of the regular diet [3, 61].

In summary Ayurvedic medicines have advantages in obesity and NAFL therapies and disadvantages due to toxicity.

Advantages of Ayurveda medications for obesity, NAFLD, and cirrhosis treatments are:

1. Wide range of options in vegetables, fruits, herbs, spice, plants, and natural animal products like honey, and lifestyle therapies for treatment.

2. Proven to be effective in treating obesity, NAFLD, and cirrhosis through various clinical trials.

3. Natural products that can be used in everyday healthy cuisines to prevent various diseases.

Disadvantages of Ayurveda medications:

1. The manufacturing practices of drugs still needs to be improved.

2. Herbs, spices, and plants contain pesticides that are required during agricultural processes.

3. Adulteration of products is possible, need care taken regarding vendor sources while purchasing the natural medications.

Ayurveda contains information on spices, herbal, natural ingredients, plants, and lifestyle therapies that originated from Indus Valley. This knowledge can be used to reduce obesity and treat NAFLD and prevent cirrhosis. Interest in the use of natural medications is growing as they are viewed as safer than processed drugs. Ayurveda prescribed medications are being tested in clinical trials to evaluate their efficacy in obesity and NAFLD. There clinical trials using Ayurvedic medications. This requires

strict regulation of manufacturing practices and quality control of Ayurveda products, in order to guarantee safety of health of consumers.

Abbreviations

BMI- body mass index
HDL-high density lipoprotein
LDL-low density lipoprotein,
MC-melanocortin
MC-4-MC-cleaved
MCP-1-monocyte chemo-attractant protein-1
NAFLD-non-alcoholic fatty liver disease
NASH-non-alcoholic steatohepatitis
PAI-1-plasminogen activator inhibitor type 1
POMC-pro-opio-melanocortin
TNF-α-tumour necrosis fact alpha
VLDL-very low density lipoprotein

Author Contributions

M. G. Neuman designed the research and wrote the paper. S. Menashi conducted the literature search and contributed to the writing of the paper. L. B. Cohen added his professional view on NAFL-NASH and therapeutic interventions. All the authors agreed with the final version of the paper.

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Competing Interests

The authors have declared that no competing interests exist.

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