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Analysis on the Anti-obesity Mechanism of Warm Drugs Based on "Yang Leading to Qi and Yin Leading to Formation"

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Abstract: ***Obesity has become one of the major health problems threatening people's health in the 21st century, the mechanism of which is the accumulation of lipid in the body caused by energy intake exceeding energy consumption. Traditional Chinese medicine has attracted attention because of its multi-target and multi-pathway treatment characteristics. Traditional Chinese Medicine believes that the fundamental pathogenesis of obesity lies in the insufficiency of both the spleen and the kidney in essence, accompanied by full of phlegm-damp. "Those who suffer from phlegm fluid should be treated with warm drugs", recorded in Jinkui yaolue. The warm drugs, which functions based on "yang leading to qi and yin leading to formation", should be used to improve the basic metabolic rate of the body, improve the function of the viscera, promote gene expression in adipose tissue, reduce insulin resistance, regulate cholesterol metabolism and improve the intestinal microbial ecosystem to achieve anti-obesity effects.***

Keywords: Obesity, Warm medicine, Yang transforms Qi, Energy metabolism, Lipid accumulation**.**

1. Introduction

Obesity refers to excessive total body fat content and/or increased local fat content and abnormal distribution, which is a chronic metabolic disease caused by the interaction of genetic and environmental factors [1]. The mechanism is that energy intake exceeds energy expenditure. Obesity is associated with an increased risk of several diseases, including hypertension, type 2 diabetes (T2D), cardiovascular disease (CVD), and certain cancers. According to the research team, by 2030, the rate of overweight (24.0 kg/ m^2 ≤BMI < 28.0 kg/ m^2) and obesity (BMI≥28.0 kg/ m2) in Chinese adults will be 65.3%, and the number of overweight and obese people may reach 789.95 million [2]. Obesity has become a major health challenge for the Chinese population.

In recent years, traditional Chinese medicine (TCM) has attracted attention due to its multi-target and multi-pathway treatment of obesity. According to traditional Chinese medicine (TCM), the fundamental pathogenesis of obesity lies in deficiency of the root and excess of the spleen and kidney Yang deficiency, and internal obstruction of phlegm dampness as the standard. Due to the excessive diet of fat, sweet, thick and greasy, the obese people lead to the endogenous phlegm dampness, which hinders the repression of spleen Yang, the spleen is disabled, and the body fluid transport is disordered. Spleen Yang deficiency is difficult to nourish-kidney Yang for a long time, which is spleen and kidney Yang deficiency. LIU Feng [3] and other scholars believe that promoting Yang to change qi and inhibiting Yin formation may be the correct idea of TCM diagnosis and treatment of obesity. "Yang transforms qi and Yin forms" comes from The Corresponding Relation Between the Yin and Yang of Man and All Things and That of the Four Seasons in Suwen. It is intended to help Yang transform qi by warming drugs, while Yin congeals and dissipates when Yang qi rises. This article summarizes the domestic and foreign scholars' research on the regulation of gene expression in adipose tissue, reducing insulin resistance, regulating cholesterol metabolism and improving intestinal microecological environment, and discusses the theory of Yang transforming Qi and Yin formation, in order to provide new ideas for the study of the anti-obesity mechanism of warm-heat medicinal herbs.

2. Etiology and Pathogenesis of Obesity

Obesity was first recorded in Huangdi Neijing, in which it was mentioned that "people like to eat sweet and fat" and "Western people tend to eat fatty food", indicating that the occurrence of obesity is related to improper diet and environmental factors. According to human skin, flesh, qi and blood, obesity is divided into three types in Neijing, meat type, fat type and paste type. Shuo Wen Jie Zi explains: "coagulated, the fat, the release of the paste." It means that the tightly packed meat is called fat, and the fluffy fat is called paste, emphasizing that the fat content determines the degree of obesity. In the Lin Shu, it is said, "When the body and fluid of the five grains are combined and become an ointment, it is infused into the bone cavity, replenished the brain and flows down into the Yin strands." It shows that ointment fat can be deposited in the subcutaneous, internal organs, abdominal cavity and blood vessels [4], which is an important part of the body's water and fluid metabolism. Ye Tianshi of the Qing Dynasty put forward, "The soft white skin of the husband is qi deficiency, the outside seems abundant, the inside is really weak, cover the body of Yang deficiency, but the phlegm and dampness..." The root cause of "cream fat" is the accumulation of phlegm and dampness in the body, which is qi deficiency and Yang deficiency in the body. Zhu Danxi pointed out: "The Yang qi of the person's health is like the day of the day, and the Yin is blocked, and the day loses its place. The spleen is like the hot sun in the sky, and the phumm is cloudy and the Yin is condensed." It also shows that the key to phlegm dampness lies in the healthy movement of the spleen and Yang. If the spleen and Yang are long deficient, there is no way to nourishthe kidney Yang, which is spleen and kidney Yang deficiency. Therefore, the basic pathogenesis of obesity lies in

the deficiency of the essence and the excess of the spleen and kidney. The deficiency of the essence is mainly spleen and kidney Yang deficiency, and the standard is phlegm dampness in the interior. Yang deficiency promotes weakness and causes body fluid metabolism disorder, forming phlegm dampness, and the accumulation of cream and fat over time leads to obesity.

3. "Yang Transforms qi, Yin Forms" Connotation and Warm Medicine

There is a saying in Suwen: "Yang transforms qi, and Yin forms." According to "Qi monism", Yin and Yang are two aspects of the nature of things that are both interrelated and opposite, and the law of yin-yang vaporization mainly lies in "Yang transforming qi" and "Yin forming". Zhang Jiebin noted in Lei jing, "Yang moves and disperses, so it melts qi; Yin is still and congesting, so it takes shape." Positive heat is active and has the characteristics of activity, warmth and invisible distribution. It can warm and promote human life activities through gasification [5]. The "Yin" cold is mainly static, which is formed by agglutination and micro-aggregation. Yin self coagulation, in the case of Yin and Yang balance, coagulation without stagnation, will not cause excessive accumulation of adipose tissue. Yang deficiency promotes weakness, body fluid metabolism disorder, phlegm dampness condensation. Synopsis of the Golden Chamber said, "Patients with phlegm and drink should be treated with warm medicine." Among them, the warm medicine refers to the medicine that tends to be warm in the four qi. The four qi, also known as the four properties, is divided into four different kinds of medicinal properties: cold, heat, warm and cool. It reflects the tendency of action of drugs on the rise and fall of Yin and Yang and the changes of cold and heat in the human body. In terms of the nature of the four qi, only cold and hot are distinguished. According to traditional Chinese medicine, cold is the most cool, and heat is the pole of warm, so there is no essential difference between cold and cool, warm and hot [6]. "Cold people are hot, hot people are cold" is the primary principle of traditional Chinese medicine (TCM), and the characteristics of cold and hot are reflected in the change of energy. Neijing said, Yang qi, if the day and the day, lose its place, then the life and not show, so the day should be bright. Neijing hold that Yang is strong and Yin is weak, Yang is dominant and Yin is subordinate, and everything in life activities needs the cooperation of Yin and Yang. The warm medicine belonging to Yang can play the role of helping Yang and warming, and improve the state of ointment and fat accumulation caused by the body's failure to promote.

4. Molecular Mechanism of the Antiobesity Effect of Warm-heat Traditional Chinese Medicine

In Suwen, it is said, "When Yin wins, Yang suffers." The essence of obesity formation is long-term lipid accumulation. Due to the excessive eating of fat, gan, thick and greasy, nourishment hinders the spleen, damages the spleen Yang, the spleen loses circulation, and the "Yang changes qi" is insufficient, resulting in too much "Yin forming", the damp turbidity stops between the skin and flesh of the viscera, blocks the movement of qi and blood, further damages Yang qi, and aggravates the pathological state of "Yin forming". The Truth of Medical theory said, Yang qi circulation, Yin qi stagnation, Yang qi deficiency, a little block, a cluster of diseases. Wenre medicine is warm, promotes the gasification of the human body, and improves the metabolic disorders mainly caused by lipid metabolism in obese people. Adipose tissue, liver, and small intestine are the main sites for lipid synthesis. Recent studies have found that thermodrugs can achieve anti-obesity efficacy by regulating gene expression in adipose tissue, reducing insulin resistance, regulating cholesterol metabolism, and improving intestinal microecological environment.

4.1 Regulation of Gene Expression in Adipose Tissue

4.1.1 It can promote "Yang to change qi", increase the expression of thermogenic genes such as UCP1, and induce the Browning of white adipose tissue.

There is a saying in the book of Nan Jing, "Qi is the master of genial warmth". Yang qi warms the human body, maintaining body temperature, normal physiological activities and the normal operation, transport and excretion of semen, blood and body fluid. At the molecular level, warm-drugs increase the thermogenesis of adipose tissue by promoting Yang and induce the Browning of white adipose tissue to improve obesity. The main adipose tissues known to exist in mammals are white adipose tissue (WAT), brown adipose tissue (BAT), and beige adipose tissue. WAT stores excess energy in the form of triglycerides, and regulates lipid metabolism by releasing various adipokines, such as leptin, adiponectin, fibroblast growth factor (FGF21), etc., through autocrine or paracrine forms [7]. In the case of cold stimulation and activation of the norepinephrine signaling pathway, BAT generates heat to dissipate energy through non-shivering fever [8]. Studies have found that when BAT thermogenesis is abnormal, the energy expenditure of mice is reduced, which is prone to obesity [9]. BAT accounts for only 4.3% of AT in adults, and neonatal interscapular BAT decreases over time and is no longer detected in adults [10]. WAT can be converted into BAT under certain conditions, and the Browning process is related to mitochondrial biogenesis. Therefore, the "Browning" of white fat (also known as "beige") is an effective and feasible strategy to fight obesity and metabolic disorders. Studies have found that the key to BAT thermogenesis is the high expression of uncoupling protein 1 (UCP1) on the mitochondrial inner membrane, which causes the uncoupling effect of electron transport in mitochondrial oxidative respiration and ATP production, thereby reducing the production efficiency of fatty acid oxidative metabolism, and a large amount of energy is emitted in the form of heat [8]. In addition, adenosine monophosphoride-activated protease (AMPK) is a key regulator of mitochondrial energy metabolism and mitochondrial biogenesis, and it has been reported that the regulatory effects of myostatin, adiponectin, and irisin on WAT Browning involve AMPK activation [11].

Tao Nie [12] et al. found that astragalus promoted thermogenesis by activating PPARγ/PGC-1α/UCP1 signaling pathway, and treated obese mice showed higher body temperature, oxygen consumption (VO2) and carbon dioxide

production (VCO2). The astragalus group did not increase the amount of exercise and food intake, but lost weight, suggesting that astragalus could prevent obesity by increasing the energy consumption of adipocytes. Jing-wen Liu [13] et al. showed that psoralpa extract can increase the phosphorylation of AMPKα1/2 and p38 to activate fat Browning, increase the activity of BAT, and increase the expression of UCP1 and other thermogenic genes to improve glucose homeostasis and protect liver steatosis to prevent obesity. The application of psoralen suggests that while WAT is Browning, it may also have a broad regulatory effect on glucose metabolism and intrahepatic metabolism. Yan-an Ding [14] et al showed that the AMPK-ACC-CPT1A pathway was activated to inhibit adipogenesis by inhibiting the expression of C/EBPα and SOAT1, resulting in a decrease in the relative content of fatty acids entering the fat synthesis pathway in WAT and a relative increase in the relative content of fatty acids entering the β-oxidation pathway. Thus, it promoted the Browning of white adipose tissue in high-fat fed mice. These results suggest that Magnolia officinalis not only increases the thermogenesis of adipocytes, but also regulates the synthesis and catabolism of fat. Kang-Yun Lu [15] et al. found that Angelica sinensis extract increased the oxygen consumption of differentiated beige adipocytes in mice by inducing β-adrenergic receptor (cAMP/PKA) and AMPK activated protein kinase (AMPK/acetyl-coa carboxylase/SIRT1) signaling pathways, and a large number of mitochondria appeared in the cytoplasm. The expressions of heat markers such as UCP1 and PGC-1α were increased, and WAT was Browning. These results suggest that Angelica sinensis may improve basal metabolic rate and obesity in mice by regulating the nervous system. Chuan-hai Zhang [16] et al. showed that Jixueteng significantly increased the activation of BAT and the expression level of thermogenic genes such as UCP1 to inhibit weight gain, which may improve glucose homeostasis and insulin resistance by up-regulating the MAPK and AMPK pathways, and at the same time improve liver steatosis and intestinal microbial composition. It is suggested that Jixueteng may not only promote energy metabolism, but also improve the dysfunction of viscera caused by long-term obesity in mice.

In conclusion, Radix astragali, Fructus psoraleae, Magnolia officinalis, Angelica sinensis and Jixueteng can promote the Browning of white adipose tissue, promote the production of heat and energy consumption, and enhance the function of "Yang and qi", thereby improving obesity.

4.1.2 It inhibits "Yin formation" and regulates the expression of synthesis and decomposition genes in adipocytes

It is recorded in Bei Ji Qian jin Yao fang, "Form is shaped by taste. If the taste is not in tune, the form will be damaged." Because obese people eat too much fat, sweet and thick food, the excess lipid in the body is difficult to be discharged in time, which induces the synthesis of adipose tissue to increase and the decomposition to slow down. Finally, the pathological products such as phlegm dampness, cream fat, and blood stasis are formed and condensed in the body, that is, excessive "Yin forming", which damages the body and leads to obesity. Warming drugs can promote the coordination of physiological functions of viscera by warming and promoting, improve body fluid transport disorders and intervene the occurrence and development of obesity. The mouse embryonic preadipocyte cell line (3T3-L1) is a 3T3 substrain obtained by cloning and isolation, which has the ability to proliferate and differentiate into mature adipocytes. It is an internationally recognized in vitro model of adipogenesis.

4.1.2.1 Down-regulating the expression of adipogenic transcription factors such as PPARγ and C/EBPα to inhibit adipogenic differentiation and proliferation

PPARγ and C/EBPα are the main transcription factors in the maturation and differentiation of adipocytes, which have anti-mitogenic effects and are essential for adipogenesis [17]. HAN Yunk-Yung [18] et al found that icariin increased AMPK phosphorylation and down-regulated the expression of PPARγ, C/EBPα and SREBP-1c, and further inhibited the mRNA levels of fatty acid synthase (FAS), acyl-coa synthase (ACS1) and ecyclin. It can effectively inhibit the lipid accumulation of 3T3-L1 preadipocytes and improve obesity. Hyung-Seok Yu et al. [19] showed that Inula inula could regulate the activation of ERK1/2 and Akt signaling pathways, inhibit the activation of early adipogenic transcription factors such as C/EBP-β and STAT3, and then inhibit the expression of C/EBP-α and PPARγ, and arrest the cell cycle in G0/G1 phase. Inhibition of lipogenesis and lipid accumulation including MCE. Wona Jee [20] et al. found that Polygalae extract could inhibit the differentiation and generation of adipocytes by up-regulating the AMPK/ACC pathway and down-regulating the MAPK/Akt signaling pathway to reduce the protein expression levels of PPARγ, C/EBPα, SREBP1c and FAS. Jing Zhou [21] et al. showed that ginsenoside F2 downregulates the expression levels of adipokines such as PPARγ, FASN and adiponectin by activating AMPK/ACC pathway, which inhibits adipogenesis in the early stage of adipogenesis and improves obesity. In addition, ginsenoside F2 also promoted mitochondrial biosynthesis in 3T3-L1 adipocytes and increased the expression of antioxidant enzymes such as SOD and GSH-Px in the liver to alleviate oxidative stress.

4.1.2.2 Inhibition of fat synthesis and promotion of decomposition

The study of Ra-Yeong Choi [22] et al showed that Polymonium multiatum significantly down-regulated the expression level of ChREBP, which is involved in the early adipogenesis, and DGAT2, which catalyzes the last step of triglyceride (TG) synthesis, and down-regulated the expression of inflammatory gene MCP1 in the epididymis white adipose tissue. The expression of thermogenic genes such as ADRB3 and PPARγ in interscapular BAT and TG catabolic enzymes such as HSL were up-regulated. After treatment, the mice lost body weight and increased insulin sensitivity. Mi Ra Lee [23] et al. showed that Zeolan extract reduced the expression of adipogenetic factors SREBP-1, FAS, SCD-1 and CD36 in a dose-dependent manner, and alleviated hepatic steatosis and elevated blood lipids caused by obesity by activating AMPK/ACC pathway and upregulating PPARα expression. Down-regulating the expression of pro-inflammatory factors such as leptin and TNF-α can improve chronic inflammation and obesity. Shalom Sara Thomas [24] et al. showed that Perilla inhibited fat synthesis by down-regulating the expression of adipogenic

genes such as PPARγ, FAS, ACC, aP2 and C/EBPα. At the same time, it may increase the expression of lipolytic genes such as ATGL, HSL, PPARα and ACOX to promote lipolysis by up-regulating the levels of adiponectin and AMPK, and partially inhibit adipocyte differentiation by reducing the level of GPDH to reduce the lipid accumulation of differentiated adipocytes and reduce body weight. Yea-Jin Park [25] et al. showed that Atractchlodes rhizoma decreases lipogenesis by reducing the expression of SREBP1, ChREBP and FAS, and increases Acox, PPARα and PGC-1α to promote fatty acid oxidation by activating AMPK/SIRT1 signaling pathway, thus preventing WAT expansion and weight gain.

4.2 Warming Yang Changes qi, Regulating qi to Treat Blood and Improve Insulin Resistance

Insulin resistance (IR) is the pathological basis of metabolic diseases such as obesity and diabetes. Shi Jinmo, a modern scholar, said: "The delicacy of the diet of people with blood sugar is also the same; If the spleen is not healthy, the sugar in the blood cannot be dispersed throughout the body." Due to the deficiency of spleen and Yang and dereliction of duty, the retention of phlegm and blood stasis in obese people leads to poisoning [26]. Tang Rongchuan put forward the concept that "those who treat blood must regulate qi, and those who eliminate blood must regulate qi" in his book Treatise on Blood Syndrome. Warm-heat drugs warm Yang, dissipate qi, promote spleen circulation, and improve insulin resistance caused by obesity.

Olefsky's research team [27] found that exosomes secreted by adipose tissue macrophages from obese mice contain mirnas and can be transferred to insulin target cells to inhibit insulin signaling and glucose tolerance by directly inhibiting the targeted gene PPAR-γ. Ji-hang Chen [28] et al. found that the extract of C. sinensis can induce ROS to activate AMPKα, leading to ACC2 phosphorylation and increase fatty acid metabolism in skeletal muscle, and induce mitochondrial uncoupling and increase energy metabolism through the activation of AMPK-PGC1α signaling pathway. By increasing the expression of GLUT4 in skeletal muscle, it can reduce blood glucose level and insulin resistance, and improve obesity and hyperglycemia in mice. Juan Su [29] et al. showed that purified RG-II polysaccharides (KMPS) from monkshoi significantly inhibited the proportion of M1 macrophages in adipose tissue and reduced the serine phosphorylation of IRS-1 in the liver by inhibiting the activation of the NF-κB pathway in insulin target tissues. Activation of the PI3K/AKT/GSK-3β pathway can restore glucose utilization and improve the inflammatory state of obese mice, thereby improving insulin resistance. Yu-jiao Yang [30] et al. showed that by reducing the activation of TGR5 pathway in intestinal endocrine cells, the extract of Buddha's hand reduced insulin and lipid levels, stimulated the secretion of glucagon-like peptide-1 (GLP-1), resisted liver lipid peroxidation in obese rats, improved glucose and lipid metabolism and insulin resistance, and protected liver function. Yu-han Meng [31] et al. found that ginsenoside F1 could bind to adrenergic receptor β3-AR, activate cAMP/PKA/CREB pathway, inhibit adipogenesis and promote lipolsis, increase the expression of UCP1 in adipocytes, promote cellular thermogenesis and WAT Browning, and improve obesity in mice. Meanwhile, ginsenoside F2 decreased fasting plasma glucose and serum insulin levels, thereby improving glucose tolerance and insulin tolerance. It is suggested that the improvement of tissue insulin resistance by ginseng may be achieved through WAT Browning.

4.3 Help Yang Tongli, Regulate Cholesterol Metabolism

As a saying in the Treasure Mirror of Eastern Medicine: "The remaining qi of the liver is discharged in the gallbladder, which is gathered into essence." Bile is produced by the transformation of essential qi of the liver. Modern medicine believes that the digestion and absorption of lipid substances mainly plays a role through the transformation of bile acid by cholesterol in the liver, and the liver is the most active organ in the human body to synthesize cholesterol. Therefore, cholesterol metabolism is the hub connecting the liver and lipid metabolism [32]. The deficiency of "Yang transforming qi" leads to unfavorable liver dispersion and reduced bile secretion, which further causes lipid accumulation. The nuclear receptor farnesoid X receptor (FXR) is the main bile acid sensor in the human body and exerts anti-obesity and thermogenic effects by stimulating FGF15 signaling in the enterohepatic circulation [33]. Cholesterol metabolism includes four main parts: endogenous synthesis, exogenous uptake, efflux and esterification [34]. Sterol regulatory element binding protein 2 (SREBP2) and two rate-limiting enzymes HMGCR and SM are the key regulators of cholesterol synthesis. NPC1L1 participates in the absorption and regulation of cholesterol, ABCA1 and other transporters mediate the efflux of cholesterol, and ACAT2 and other transporters can be activated by cholesterol and then catalyze the esterification of various sterol analogues [35].

Shun Hao [36] et al. showed that Eu 仲 leaf extract reduced lipid accumulation by reducing oil red O staining, increasing TC and TG secretion, and inhibiting the expression of AMPKa2, CYP7A1, ABCA1, SREBP2 and HMGCR genes, demonstrating the beneficial effect of eu 仲 leaf extract on cholesterol metabolism. Zeynep Tuzcu [37] et al. showed that cinnamomum polyphenol extract improved free fatty acid and blood lipid levels by down-regulating the expression of fatty acid transcription factors such as SREBP-1c and LXRs and bile acid enzymes such as ACLY and FAS in the liver, and by down-regulating the expression of inflammatory factors such as NF-κB. Cinnamomum polyphenol extract can improve the oxidative stress of the liver by up-regulating antioxidant dependent proteins such as NRF2 and HO-1. At the same time, cinnamomum polyphenol extract can also reduce insulin level and increase insulin sensitivity by up-regulating insulin stimulating signal factors such as PPARα and IRS-1, which has a certain regulatory effect on obesity. Ming Gu [38] et al. found that Schisandra chinensis extract may improve metabolic syndrome (MetS) by stimulating FXR signaling, up-regulate the expression of fatty acid oxidation genes in the liver such as SHP, PPARα, CPT1α and ACOX1, change the structure of bile acid pool, and inhibit the accumulation of total bile acids in the liver. At the same time, it can significantly increase the expression of thermogenic genes Dio2 and Acox1 in BAT, thereby improving obesity, hepatic steatosis and metabolic syndrome (MetS) in DIO mice. Wenyu Zhao [39] et al. showed that nutmeg extract reduced the level of liver inflammation and lipid accumulation by

inhibiting the NF-κB pathway, down-regulating the expression of downstream cytokines TNF, IL-6, IL-1β and aryl hydrocarbon receptor (AhR) -mediated FAS-SREBP 1c pathway. In addition, nutdamom can also improve the abundance of Akkermansia, Blautia and other probiotics in the intestinal flora to regulate intestinal tryptophan metabolism to help mice lose weight and inhibit inflammation. Pintu Miah [40] et al. showed that cumin significantly reduced HF diet-induced glucose intolerance, wet weight of epididymal and mesenteric fat, and blood lipid levels. Cumin decreased the levels of oxidative stress parameters such as TBARS, NO and APOP by restoring the level of reduced glutathione and increasing the activities of antioxidant enzymes such as SOD and catalase in the liver of HFD rats. In addition, it restored normal plasma ALT, AST and ALP enzyme activities, reduced cholesterol levels, reduced fat droplet deposition in the liver, and improved dyslipidemia, oxidative stress and liver injury in obese rats.

4.4 Warming Yang Invigorates the Spleen and Improves the Intestinal Microecological Environment

The intestinal flora is involved in the catabolism and storage of a variety of nutrients in the human body, and is an indispensable part of the spleen's main transportation and metabolism. Warming drugs can improve the intestinal microecology by promoting the spleen Yang and improving the intestinal microecology to obtain the anti-obesity effect. The intestinal microecosystem is the largest microecosystem in the human body. As the core part of intestinal flora, the number of intestinal flora can reach 1013-1014, which maintains intestinal homeostasis through interactions with nutrient metabolites and host cells [41]. The ratio of Firmicutes to Bacteroidetes (F/B) often indicates the change of gut microbiota. The F/B ratio has been used as a marker of intestinal microbial dysbiosis and an indicator of obesity [42]. Firmicutes include many bacteria known to produce short-chain fatty acids (SCFAs), and an increase in F/B is expected to improve the efficiency of polysaccharide fermentation to produce SCFAs [43]. Studies have shown that SCFAs can prevent obesity by increasing energy expenditure and appetite control [44], and can also reduce lipid accumulation and hepatic steatosis and increase insulin sensitivity by reducing the expression of PPARγ [45]. The mechanism of action may be achieved by regulating intestinal hormone secretion through the microbe-gut-brain axis [46].

Mengjie Li [47] et al showed that the addition of clove extract eugenol significantly increased the proportion of Firmicutes, reduced Bilophila and other bile tolerant microorganisms, increased probiotics to improve the composition and function of intestinal microorganisms, and significantly reduced HFD-induced obesity by activating the cAMP pathway. It reduces WAT hypertrophy and lipid accumulation, and blood lipid levels reduce HFD-induced obesity in mice by improving the composition and function of gut microbiota, which is manifested as weight loss and adipocytes reduction. Jun-Yan Xiang [48] et al. showed that litchi kernels could reduce the proportion of positive lipid metabolism-related microorganisms such as Cetobacterium, Aspergillus and Rhodotorula in the intestine of obese zebrafish, reduce the accumulation of TG in the liver and the expression levels of lipid metabolism genes such as PPARγ and AMPKα. At the same time, by enriching beneficial bacteria such as Trichococcus and Aeromonas, it increases the synthesis of SCFAs, regulates appetite, and is beneficial to intestinal health. The addition of litchi nucleus can reduce the proportion of Micrococcaceae and Staphylococcus causing intestinal injury and the proportion of Candida inducing liver injury, inhibit the levels of Nr3c1, bax, bcl-2 and other apoptosis-related genes in the liver and intestinal tract, reduce the serum LPS level and inflammatory response, and improve the intestinal barrier. In addition, litchi nucleus regulates cAMP signaling pathway, improves insulin resistance and affects glucose and lipid metabolism in obese zebrafish. Ecn-ji Song [49] et al. found that ephedra inhibited appetite and regulated energy metabolism by improving the relative abundance of Oscillospiraceae, Lachnospiraceae and F/B, restoring the ABC transporter pathway and the production of SCFAs in obese mice. In addition, amplicon sequence variations (ASVs) of nine gut microbes were significantly restored after ephedra treatment, of which eight ASVs were associated with body weight and fat accumulation. Jing Wang [50] et al. showed that ginger improved insulin sensitivity, OGTT, ITT, and reduced serum TNF-α and IL-6 concentrations in HFD mice by increasing PPARα/γ and NF-κB activity, thereby reducing WAT mass and liver macrophage infiltration, improving steatosis, and reducing obesity. In addition, ginger supplementation adjusted the composition of gut microbiota, increased the constituent ratio of probiotic Bifidobacterium genus and SCFA-producing bacteria Alloprevotella and Allobaculum, and increased the SCFA concentration in feces. The fecal microbiota transplantation (FMT) experiment showed similar anti-obesity and microbiota-regulating effects of oral ginger.

5. Discussion

Obesity is a chronic metabolic disease caused by the interaction of genetic and environmental factors. Excess lipids are not only stored in adipose tissue, but also accumulated in blood vessels or other organs, resulting in multi-system metabolic disorders, especially abnormal glucose and lipid metabolism in fat, liver, small intestine and other tissues and organs involved in fat synthesis. Because these effects do not occur independently, the multi-target and multi-pathway therapeutic characteristics of traditional Chinese medicine provide new ideas for the prevention and treatment of obesity. Traditional Chinese medicine emphasizes the "holistic concept", and "Yang transforming qi" is inseparable from "Yin forming", which is stated in the Neijing: "Yang is outside, Yin is in, and Yang is in." Warm medicine through warm Xuhe promoting effect, help Yang and qi, can achieve the anti-obesity effect through two points: (1) improve the basal metabolic rate of the body: It can promote the expression of thermogenic genes in white adipose tissue, increase the body's energy consumption, regulate the composition ratio of intestinal flora to increase the content of short-chain fatty acids and other metabolites involved in regulating the body's energy metabolism, and change the physiological phenomenon of low energy consumption caused by obesity. (2) Improve the function of viscera: It can improve the function of fat, liver, small intestine and other tissues and organs, promote the decomposition of fat and inhibit the formation of fat to improve the accumulation of phlegm and dampness in the body, promote water metabolism,

regulate cholesterol homeostasis, reduce the accumulation of lipids in the liver, and restore the function of liver as the main channel of blood, and reduce the body's insulin resistance. It can increase the content of intestinal probiotics to help spleen transportation. To improve the spleen and kidney Yang deficiency caused by long-term obesity, and to achieve the effect of treating obesity from the fundamental pathogenesis. Modern medicine also has some new understanding of the "holistic concept" in the treatment of obesity. En-yuan Cao [51] et al. found through experiments that intestinal lymphatic dysfunction is a potential cause of obesity and insulin resistance. Salwan Maqdasy [52] et al. demonstrated that the reduction of phosphocreatine metabolism in white adipocytes promotes pro-inflammatory responses in human in vitro and mouse in vivo obesity models. Omer Keinan [53] et al. found that glycogen metabolism can regulate fat consumption. Katsumi Iizuka [54] et al. suggested that gut microbiota, liver and adipose tissue jointly participate in ChREBP-mediated lipid metabolism, and the mechanism is to control the transcription of lipogenic enzymes and liver-derived cytokines. By regulating Yang qi and forming Yin, warm-heat medicine treats obesity from a holistic perspective and takes into account both specimens, which provides a new idea for the treatment of obesity.

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