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Research Progress of Improving Insulin Resistance of Diabetes Mellitus with Chinese Herbal Monomer

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Abstract

In recent years, large-scale clinical trials have confirmed that Traditional Chinese Medicine (TCM) has made progress in controlling blood sugar levels. Studies have found that TCM monomers play a significant role in the regulation of insulin resistance-related signaling pathway proteins. Therefore, Chinese and foreign scholars have conducted a lot of studies on the mechanism of insulin resistance. This paper integrates the studies on insulin receptor resistance of TCM (Rhizoma Alismatis, Scutellaria baicalensis, the root of kudzu vine, berberine, Cortex Moutan), and provides a useful reference for the treatment of metabolic diseases such as type 2 diabetes.

Keywords: Traditional Chinese Medicine(TCM), insulin, diabetes

1. Introduction

Type 2 diabetes is a metabolic disease characterized by high blood sugar. According to epidemiological surveys, 5.2 million people die of diabetes worldwide, with a mortality rate of 82.4 per 100,000, making it the seventh leading cause of death worldwide. The incidence of metabolic syndrome in China has reached 33.9%(31.0% in males and 36.8% in females) and is increasing year by year, seriously affecting people's lives (Glovaci, D., Fan, W., & Wong, N. D., 2019). It is estimated that by 2030, the number of diabetes patients in China will reach 140 million. It is estimated that by 2045, the prevalence of diabetes will rise to 12.2%, and the number of cases will increase to 783 million (Guo Lixin). The prevalence of diabetes in adults increases with age. The prevalence rate was the lowest among 20-24 year-olds (1.4%). In the middle-aged population, the prevalence rate of all ages increases rapidly; The prevalence rate is as high as 20% in people 65 and older. Among diabetics aged 20-79, nearly three-quarters are of working age (< 65). The trend is expected to remain similar over the next 25 years (2019).

Diabetes does great harm to human health, so it is urgent to find an effective way to treat type 2 diabetes. Studies have shown that treating insulin resistance is an important step in reducing the risk of type 2 diabetes. Therefore, insulin resistance has always been a hotspot of multidisciplinary research in the medical field. Insulin resistance in the overall situation is due to a lack of insulin receptor and insulin receptor defects after the physiological concentration of unable to maintain blood sugar at normal levels, namely the target tissue response to insulin sensitivity decreases, and a certain concentration of insulin cannot make cells reached its corresponding metabolism, only improve the level of insulin concentrations can achieve expected metabolism, Therefore, patients with insulin tolerance are often accompanied by hyperinsulinemia. Insulin resistance may be one of the major culprits of various metabolic diseases, and its metabolic signaling pathways are crucial for maintaining homeostasis. Many scholars have proved through practice that some Traditional Chinese medicines, such as Alisma, radix puerariae, Coptis Chinensis, cortex moutan, and Scutellaria baicaleae, play an important role in improving insulin resistance. This paper integrates traditional Chinese medicine monomers that can improve

insulin resistance, providing a beneficial reference for the treatment of metabolic diseases such as type 2 diabetes.

2. Rhizoma Alismatis

Zhou Yi et al. (Zhou Y & Na L X.) found that Alisma's anti-T2DM is related to biological processes such as cell migration, metabolism, signal transduction, and receptor activation. Zm plays a direct or indirect therapeutic role through the coordination of ErbB signal transduction pathway, insulin resistance pathway, and insulin signal transduction pathway related to diabetic complications. It has a significant effect on lowering blood glucose and blood lipids. Danshen Jiangtang capsule containing Alisma can improve the blood glucose level of diabetic patients and protect the B cells of islet (Fang ZHAOhui & Chen Zhi, 2019), proving that Alisma can improve the qi and Yin deficiency and blood stasis syndrome of T2DM. Zhang Chunhai et al. (Zhang C H, MAO Z & MA L, et al, 2015) found through animal experiments that Alisma can lower blood lipid by reducing liver cholesterol synthesis. Zhang Weiyun et al. ingavaged T2DM mice with different doses of xiexene, and found that Xiexene promoted 3T3-L1 preadipose differentiation, which may be conducive to enhancing insulin sensitivity, and decreased FBG and blood glucose in T2DM mice during oral glucose tolerance test. At the same time, they also concluded that 23-acetynol B can improve insulin sensitivity, improve insulin resistance, and ultimately reduce glucose concentration (Zhang Weiyun, Liu Huaxin & Wang Qing, et al., 2019).

3. Scutellaria Baicalensis

It is reported that the treatment of scutellaria baicalensis and its active component baicalin can significantly reduce the blood glucose level of type 2 diabetic rats, indicating that scutellaria baicalensis has a definite hypoglycemic effect. It was also found that baicalin, baicalin, and baicalin in Scutellaria can significantly increase the glucose consumption of insulin-resistant HepG2 cells (Zhu Shuilan, Wu Qinghua & Tu Xu, 2019), and baicalin can also increase the content of liver glycogen in diabetic rats. However, baicalin in Scutellaria can significantly reduce the lipid accumulation of HepG2 cells stimulated by palmitic acid. It was also found that scutellaria extract significantly upregulated the phosphorylation of PI3K and Akt of IRS-1, PI3K, AkT-2, and Glut-2 gene and glut-2 protein expression in the liver of type 2 diabetic rats, thus improving insulin resistance and playing an anti-type 2 diabetes role (CUI X, QIAN D W & JIANG S, et al., 2018). Zheng Xiaopeng et al. (Zheng Xiaopeng, Feng Jing & Song Chaoyu, et al., 2020) found that baicalin can decrease blood glucose, delay the progression of diabetic nephropathy, improve insulin resistance and improve renal fibrosis, and its mechanism may be closely related to the regulation of transforming growth factor -β1 expression by baicalin.

4. The Root of Kudzu Vine

Pharmacological experiments have proved that puerarin can inhibit platelet aggregation, reduce plasma endothelin, effectively block β adrenal receptors (Han HUi-min & WANG Shu-guo, 2006), and also reduce blood pressure and blood viscosity, which can effectively improve blood circulation (Sun W, XU Q L & ZHENG X Z, et al., 2007). In Zhang Hongmei's study, after puerarin intravenous infusion, the insulin sensitivity index and insulin resistance index of the observation group were improved, and significantly better than the control group of conventional treatment, indicating that puerarin can effectively improve the effect of insulin resistance. This conclusion was also proved in the studies of Wei Shuqin (Wei S Q., 2017), Yu Jian et al. (Yu J, 2001). Yang Lei et al. (Yang Lei, Shu Ming & Yao Dongdong, et al., 2014) administered puerarin orally, FBG decreased, FINS increased, the number of β cells increased, and the level of P-Akt in the liver increased in the puerarin group. Therefore, the hypoglycemic mechanism of puerarin may be related to the protection of pancreatic β cells and the activation of insulin receptor downstream AKT pathway by improving liver function. Gao Junfeng et al. (Gao Junfeng, Liu Manman & Guo Zhaoping, et al.) further study found that puerarin inhibited hepatic ACC mRNA expression in a dose-dependent manner, and puerarin may reduce insulin resistance in T2DM mice by regulating the hepatic ACC signaling pathway, and further improving glucose and lipid metabolism.

5. Berberine

Modern pharmacological studies have confirmed that mitochondrial dysfunction can cause insulin resistance, and the bidirectional regulation of berberine on mitochondrial function inhibition and activation can improve insulin sensitivity (Yong Zhang & Jianping Ye, 2012), and also increase the expression levels of glucose transporter protein (GLUT-4) and glucagon-like peptide-1 (GLP-1). Improve cell glucose absorption and participate in the activation of the adenosine-activated protein kinase (AMPK) signaling pathway, thereby reducing blood glucose and insulin resistance (Cicero Arrigo F G & Tartagni Elisa, 2012). However, the age of patients, daily dosage of berberine, treatment duration, and other factors will affect the hypoglycemic effect (Li Cheng, He Jinzhi & Zhou Xuedong, et al., 2017). One study suggested that berberine can reduce fasting glucose, 2 h postprandial glucose, and glycosylated hemoglobin levels in type 2 diabetic patients with insulin resistance. In terms of lowering insulin resistance index, the reduction of HOMR-IR was stable and reliable in

the berberine single dose > 0.3g group, while the heterogeneity was obvious in the berberine dose ≤0.3 g group. The effect of reducing HOMR-IR should be treated with caution, suggesting that different berberine dose may affect the treatment (Xin Ke, Deng Xiaoge, Yuan Jiayao & Feng Zhihai, 2020). Huang Y F et al. (Huang Yunfang, Shan Hezhen & Zhang Ting, et al., 2020) found that both berberine and berberine could reverse the activity of tryptophan hydroxylation 1 (TPH1) in pancreatic β cells of T2DM mice, while berberine inhibited the activity of TPH1 in colon tissue of T2DM mice. TPH1 mainly controlled the synthesis of peripheral 5-hydroxytryptamine, and TPH inhibitors inhibited the synthesis of 5-hydroxytryptamine and blocked the proliferation of β cells. Glucose intolerance was induced in pregnant mice.

6. Cortex Moutan

Recent studies have shown that the occurrence and development of diabetes mellitus are closely related to the inflammation of microvessels. The basal levels of inflammatory mediators C-reactive protein (CRP), tumor necrosis factor (TNF), and interleukin-6 (IL-6) were significantly correlated with the occurrence and development of diabetes. Studies have found that cortex moutan can reduce the levels of CRP, TNF, and IL-6 in the blood of diabetic patients, indicating that cortex moutan has the function of resisting the inflammatory reaction of diabetes and protecting vascular endothelial cells (Min C Y., 2009). Wang Qin-mao et al. (Wang Qinmao, Hong Hao & Zhao Zhiping, et al., 2002) found that polysaccharides from cortex pedantifoliae could reduce FBG and improve glucose tolerance by increasing the maximum binding capacity of low-affinity insulin receptors in liver cells, increasing insulin sensitivity index, and improving insulin resistance.

7. Conclusion and Outlook

Clinical diseases related to insulin resistance include cardiometabolic diseases, stroke, Alzheimer's disease, polycystic ovary syndrome, cancer, and so on, among which the suffering of diabetic patients due to insulin resistance is particularly prominent. Western medicine side effects brought by the sodium water retention, weight gain, and abnormal liver function, it is worth noting that Chinese traditional medicine drugs can significantly reduce this kind of phenomenon occurs, significant advantages in the treatment of diabetes mellitus of Chinese medicine, for some effect and side effects of traditional Chinese medicine mining is an important way of promoting the innovation of drug discovery, in the hope that the future research, More Chinese medicines could be found to target insulin resistance mechanisms.

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