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ORIGINAL RESEARCH

Resistant Dextrin Protects Rats Against Streptozotocin Induced Gestational Diabetes Mellitus via Alteration of TLR4/MyD88/NF-κB Signaling Pathway

Shuijing Wang, MD; Liangkun Ma, MD; Jing Ji, MD; Ruichao Huo, MD; San Dong, MD; Yunfeng Bai, MD; Linlin Hua, MD; Yan Yu, MD

ABSTRACT

Objective • Gestational diabetes mellitus (GDM) is a metabolic disorder that occurs in 3–5% of pregnancies. The inflammatory response is essential to the development of GDM. Resistant dextrin is a natural fiber and exhibits an antidiabetic effect against diabetes. We investigate resistant dextrin's preventive role and underlying mechanism against STZ-induced GDM.

Material and method • Female Wistar rats were utilized, and GDM was induced in pregnant rats using STZ. The levels of glycated hemoglobin (HbA_{1c}), resistin, serum-c-peptide, free fatty acid, antioxidant, hepatic glycogen, lipid, inflammatory cytokines, apoptosis, and inflammatory parameters were estimated. mRNA expression of Toll-like receptor 4 (TLR4), myeloid differentiation primary response 88 (MyD88), nuclear factor kappa B (NF-κB) and NOD-like receptor protein 3 (NLRP3) was estimated. We also estimated the histopathology of pancreatic and liver tissue.

Result • Body weight, plasma insulin, fetal body weight, and blood glucose levels were all considerably ($P < .001$) improved by resistant dextrin, while placental weight and blood sugar levels were also decreased. Resistant dextrin significantly ($P < .001$) suppressed the levels of HbA_{1c}, resistin, serum-c-peptide, and hepatic glycogen and improved the free fatty acid (FFA) level. Resistant dextrin significantly ($P < .001$) altered the level of adiponectin, leptin, intercellular Adhesion Molecule 1 (ICAM-1), and visfatin; antioxidant parameters such as malonaldehyde (MDA), superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), glutathione peroxidase (GPx), glutathione S-transferase GST, inflammatory cytokines like tumor necrosis factor- α (TNF-α), interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-2 (IL-2), interferon- γ (INF-γ), interleukin-10 (IL-10); apoptosis parameters include Bcl-2, caspase-3, and Bax, respectively. Resistant dextrin significantly ($P < .001$) suppressed the mRNA expression of NF-κB, MyD88, NLRP3, and TLR4. Resistant dextrin altered the histopathological changes in the pancreas and hepatic tissue.

Discussion & Conclusion • In short, resistant dextrin demonstrated a protective effect against STZ-induced GDM by modulating the TLR4/MyD88/NF-κB signaling pathway. (*Altern Ther Health Med.* 2024;30(12):65-71).

Shuijing Wang, MD; Yan Yu, MD; School of Public Health, Xi'an Jiaotong University, Xi'an Shaanxi, China. **Liangkun Ma, MD;** Department of Obstetrics and Gynecology, National Clinical Research Center for Obstetric & Gynecologic Diseases, PUMC Hospital, CAMS and PUMC, Beijing, China. **Jing Ji, MD;** Northwest Women's and Children's Hospital, Xi'an Shaanxi, China. **Ruichao Huo, MD;** Pingyao Agriculture and Rural Bureau, Pingyao Shanxi, China. **San Dong, MD;** Nutritional department, Maternal and Child Health Care Hospital of Hai Dian District, Beijing, China. **Yunfeng Bai, MD;** School of Public Health, Shaanxi University of Chinese Medicine, Xianyang, China. **Linlin Hua, MD;** Department of Advanced Medical Research, The Second Affiliated Hospital of Zhengzhou University, Jinshui district, Zhengzhou, China.

Corresponding author: Yan Yu, MD
E-mail: yanyuxjt@hotmail.com

INTRODUCTION

One type of diabetes that appears during pregnancy is called gestational diabetes mellitus (GDM).[1] It affects about 2-10% of pregnancies and is usually detected between weeks 24 and 28 of pregnancy. About 3% to 25% of pregnancies worldwide are affected by GDM, and its prevalence is rising as a result of higher risks of both short- and long-term problems, as well as unfavorable outcomes for both mothers and children, such as diabetes mellitus, especially type 2, and other metabolic dysfunctions.[2,3] It represents a pre-diabetic state, displaying a range of pathophysiological features akin to type 2 diabetes, including hyperglycemia, hyperlipidemia, biochemical dysfunction, and insulin resistance.[4] Earlier reports indicate that abnormalities in vascular endothelial cells (VECs) and microvascular cells occur in the umbilical cord and placenta in GDM, potentially contributing to an augmented risk of cardiovascular diseases, both in the immediate and long-term (He and Wu 2021). Endothelial

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dysfunction is a key factor in the pathophysiology of several metabolic illnesses associated with pregnancy, including GDM, pregnancy-related hypertensive disorders, obesity, and hyperlipidemia.[4] During the pregnancy, the endothelium undergoes significant changes to accommodate the increased demand for blood flow to the developing foetus.[6,7] Therefore, these changes may lead to endothelial dysfunction, typified by decreased nitric oxide (NO) bioavailability and poor endothelial function. These effects can lead to diminished vasodilation, heightened vascular resistance, and compromised glucose and lipid metabolism, all of which may contribute to the onset of metabolic disorders, including GDM, hypertensive disorders of pregnancy, obesity, and hyperlipidemia.[7,8] Endothelial dysfunction is believed to stem from various factors, including oxidative stress, inflammation, and insulin resistance.[9,10] Endothelial dysfunction may manifest prior to pregnancy, potentially predisposing women to the onset of hypertension during pregnancy and preeclampsia. Preeclampsia is a potentially fatal condition marked by high blood pressure and harm to several organ systems, such as the brain, liver, and kidneys.[9,11] Although endothelial dysfunction plays a crucial role in the etiology of GDM and other pregnancy-related metabolic disorders, the exact mechanism by which VEC damage and dysfunction occur during GDM is yet unknown.[5] Furthermore, there is a lack of data on effective interventions that can protect women with GDM and their offspring against cardiovascular risks associated with endothelial dysfunction. To better understand the pathogenesis of GDM and endothelial dysfunction and to find effective therapeutic and preventive interventions, more study is required.[9]

Both GDM and T2DM share similar pathological characteristics, encompassing an insulin-resistant state and chronic inflammation. In both conditions, the body experiences reduced responsiveness to insulin, resulting in elevated blood sugar levels.[12] According to certain research, the development of insulin resistance and high blood sugar in patients with GDM may be facilitated by the production of inflammatory cytokines mediated by TLR4.[13,14] TLR4 is a crucial receptor in the immune response, responsible for recognizing and responding to pathogens. When activated by specific molecules, Chronic inflammation is facilitated by TLR4-induced production of pro-inflammatory cytokines, including TNF-α and IL-1β. Research has revealed that elevated TLR4 and its cytokines downstream are linked to GDM and insulin resistance.[12-14] Furthermore, it has been demonstrated that TLR4-mediated inflammation affects skeletal muscle cells' and adipocytes' insulin signaling and glucose uptake. Targeting the Toll-like receptor 4 (TLR4)/MyD88/NF-κB pathway may be a viable therapeutic approach for the prevention and treatment of GDM, as it is thought to play a critical role in the development of inflammation.[12,15]

According to the study's hypothesis, resistant dextrin controls TLR4 expression to have anti-inflammatory and hypoglycemic effects. The in vivo tests, which sought to describe the mechanisms and effects via which TLR4 regulates insulin expression in GDM rats, were centered on the inflammatory response. Thus, targeting TLR4 and its downstream signaling pathways may be a promising therapeutic strategy for the prevention and treatment of GDM as well as other inflammatory and metabolic illnesses.

MATERIAL AND METHODS

Rodent

In the current experimental study, Sprague Dawley (SD) rats were utilized, comprising 30 females and 15 males, with an average weight of approximately 180±20 g. All rats were housed in standard laboratory conditions, maintaining a controlled temperature (20±5°C), relative humidity (65%), and a 12/12-hour dark and light cycle. The rats had ad libitum access to a standard diet and water. After acclimatization for 7 days, mating was allowed for both female and male rats. Pregnancy in female rats was confirmed by the presence of a copulatory plug the next morning, designating this day as gestational day (GD 0).[4]

STZ and nicotinamide

In brief, STZ at a dose of 55 mg/kg was prepared by dissolving it in citrate buffer solution (pH=4.5),[17,18] and nicotinamide was dissolved in the normal saline.[15]

GDM model

Following pregnancy confirmation, the rats were split up into three groups, each with six rats. The normal group rats received saline treatment throughout the entire experimental study. Another set of pregnant rats was employed for the induction of diabetes, utilizing STZ at a dose of 55 mg/kg administered intraperitoneally. The rats were given oral nicotinamide (110 mg/kg) dissolved in normal saline after receiving STZ.

Rats with blood glucose levels greater than 10 mmol/L on the fourth day of gestation were designated diabetic controls. One diabetic group received oral administration of resistant dextrin (20 mg/kg per day) for 2 weeks. All groups of rats were executed at the conclusion of the third week (19th day) of the gestation period, and blood samples were obtained via retro-orbital puncture. The blood was then centrifuged to separate plasma for biochemical parameter estimation. Additionally, pancreas and liver tissues were collected for histopathological analysis. A group of pregnant rats was observed until they gave birth to evaluate the effect of the medication on GDM and litter size.

Biochemical analysis

The oxidative stress parameters like MDA, GPx, CAT, GST, GSH, and SOD were estimated using the kits in the tissue and serum via following manufacture instructions (Cayman Chemicals, USA).

The lipid parameters like total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C), and triglyceride (TG) were determined using the biochemistry auto-analyzer (HP-CHEM300, Auto Biochemistry Analyzer). The levels of

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LDL-C and VLDL-C were estimated using the previously reported formula.[16,18] The ELISA kit (Fine Biotech, China) was utilized to estimate the inflammatory cytokines, namely TNF-α, IL-1β, and IL-6, in accordance with the manufacturer's instructions. Resistin and insulin levels were estimated using the ELISA kits following (RayBiotech, Inc, USA) the manufacturing instructions.

Following the manufacturer's instructions, the ELISA kit (Nanjing Jiancheng Bioengineering Institute, Nanjing, China) was utilized to evaluate apoptotic indicators, including caspase-3, Bcl-2, and Bax.

PCR analysis

We evaluated the mRNA expression in each group in order to clarify the molecular mechanism. Using the TRIzol reagent, total RNA was extracted from the liver tissues of every group of rats. The total RNA extraction involved a series of steps, including solvent precipitation using chloroform, ethanol, and isopropanol. A NanoDrop spectrophotometer was used for the quantification, and known quantity of can was synthesized using the iScript cDNA synthesis kit by following the manufacturer's instructions. Real-time PCR, utilizing the SYBR Green PCR Master Mix kit, was employed for the amplification of specific genes following the manufacturer's instructions (Applied Biosystems, Life Technology, USA). Table 1 lists the primer sequences used in the investigation. The Ct values were utilized to calculate the fold enhancement in gene expression. The comparative Ct method (ΔΔCt) was utilized to quantify gene expression, with GAPDH expression values acting as the internal reference.

Histopathological evaluation

Hematoxylin and eosin were used to stain the pancreatic and liver tissue after being sectioned into small (5 μm) pieces and preserved in paraffin.

Statistical analysis

To perform statistical analysis, GraphPad Prism 7.0 (St. Louis, USA) was utilized. The standard error of the mean, or mean±SEM, is used to present all data. The *t* test was used for two-sample comparisons, and one-way ANOVA was used for comparisons involving several groups. $P < .05$ was used as the statistical significance level.

RESULTS

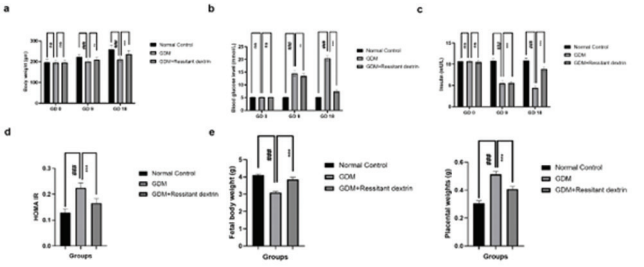
Body weight, placental weight, fetal weight, Plasma insulin, blood glucose, and HOMA-IR

ody weight is considered to be the one parameter for the estimation of diabetes: GD 0, the body weight of all groups is almost similar and insignificant. Rats in the resistant dextrin group showed a substantial ($P < .01$) increase in body weight at gestational day (GD) 9, whereas the rats in the GDM group showed a significant ($P < .001$) decrease in body weight. By GD 18, the GDM group rats exhibited a decrease in body weight, whereas the resistant dextrin group showed an improvement in body weight. Figure 1 illustrates the suppressed fetal weight in the GDM group rats, and resistant dextrin treatment significantly ($P < .001$) enhanced fetal weight. Figure 1 shows the improved placental weight in the GDM group rats, and resistant dextrin significantly ($P < .001$) decreased placental weight.GDM group rats exhibited elevated glucose levels at GD 9 and GD 18, and resistant dextrin significantly ($P < .001$) suppressed glucose levels (Figure 1). Plasma insulin, an important parameter for assessing diabetic conditions, is typically suppressed during diabetes. GDM group rats showed similar results at GD 9 and 18. Resistant dextrin significantly ($P < .001$) improved plasma insulin levels (Figure 1). Figure 1 demonstrates the increased level of HOMA-IR and resistant dextrin significantly ($P < .001$) suppressed HOMA-IR levels.

Table 1. List of primers

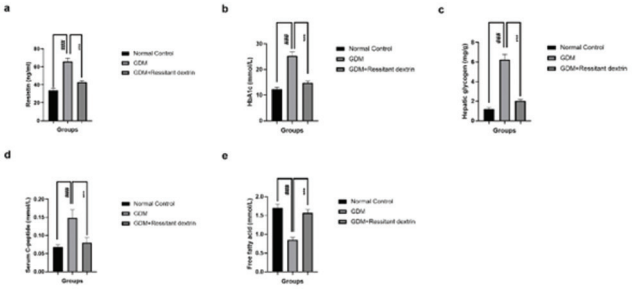
S. No	Primer	Primer Sequences (5'-3')	
		Forwarded	Reverse
1	TLR4	CTGCAGGTGCTGGATTTATCC	GGTGGCTTAGGCTCTGATATGC
2	NLRP3	TACGGCCGTCTACGTCTTCT	CGCAGATCACACTCCTCAAA
3	MyD88	ACTGCTCGAGCTGCTTACCAA	CTCCTGCTGCTGCTTCAAGAT
4	NF-KB	CCCATCTTTGACAATCGTGC	CTGGTCCCGTGAAATACACC
5	GAPDH	AGTGCCAGCCTCGTCTCATA	GATGGTGATGGGTTTCCCGT

Figure 1. showed the effect of resistant dextrin on the body weight, fetal, placental weight, blood glucose level, insulin, and HOMA IR against the STZ-induced GDM in rats. **a:** Body weight, **b:** blood glucose level, **c:** insulin, **d:** HOMA IR, **e:** fetal weight, and **f:** placental weight. All the data showed as means ± standard error of the mean (SEM).



###Significant variation at $P < .001$
***Significant variation at $P < .001$

Figure 2. showed the effect of resistant dextrin on the resistin, HbA_{1c}, hepatic glycogen, serum C-peptide, and free fatty acid against the STZ-induced GDM in rats. **a:** resistin, **b:** HbA_{1c}, **c:** hepatic glycogen, **d:** serum C-peptide and **e:** free fatty acid. All the data showed as means ± standard error of the mean (SEM).



###Significant variation at $P < .001$
***Significant variation at $P < .001$

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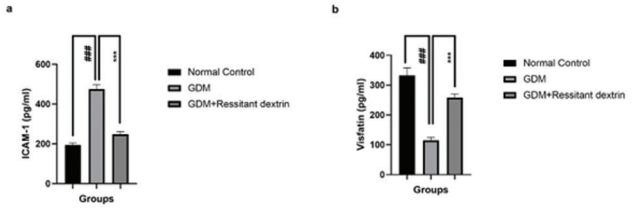
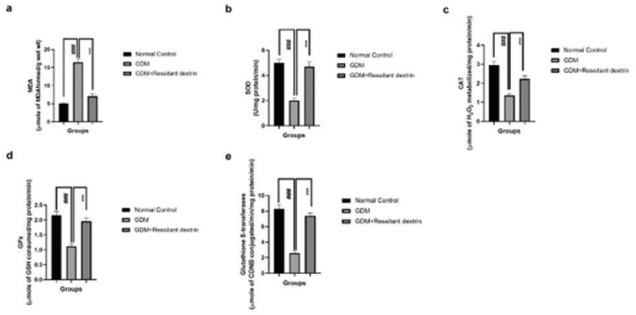
Figure 3. Showed the effect of resistant dextrin on the ICAM-1 and visfatin against the STZ-induced GDM in rats. **a:** ICAM-1 and **b:** visfatin. All the data showed as means ± standard error of the mean (SEM).



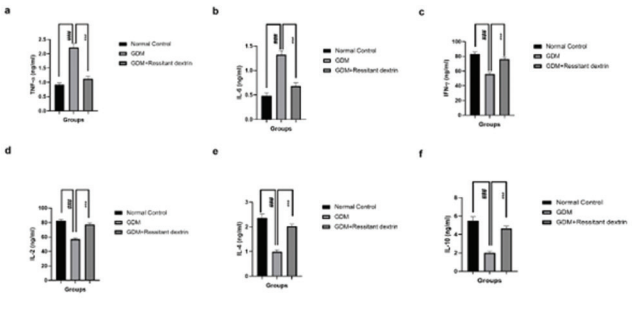
###Significant variation at $P < .001$
***Significant variation at $P < .001$

Figure 4. Showed the effect of resistant dextrin on the antioxidant parameters against the STZ induced GDM in rats. **a:** MDA, **b:** SOD, **c:** CAT, **d:** GPx and **e:** GST. All the data showed as means ± standard error of the mean (SEM).



###Significant variation at $P < .001$
***Significant variation at $P < .001$

Figure 5. Showed the effect of resistant dextrin on the proinflammatory cytokines level against the STZ induced GDM in rats. **a:** TNF-α, **b:** IL-6, **c:** IFN-γ, **d:** IL-2, **e:** IL-4 and **f:** IL-10. All the data showed as means ± standard error of the mean (SEM).

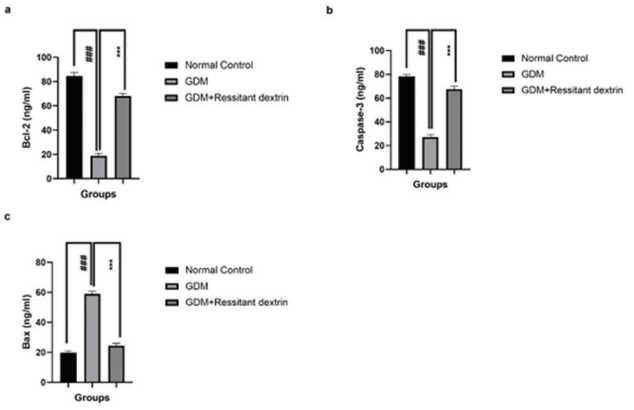


###Significant variation at $P < .001$
***Significant variation at $P < .001$

Resistin, free fatty acid, hepatic glycogen, HbA_{1c}, and serum-C-peptide

GDM rats exhibited significantly ($P < .001$) improved levels of resistin (figure 2a), HbA_{1c} (figure 2b), hepatic glycogen (figure 2c), serum-c-peptide (figure 2d), free fatty acid (figure 2e) as compared to without treated rats. GDM rats treated with resistant dextrin significantly ($P < .001$) altered the level of resistin, HbA_{1c}, hepatic glycogen, serum-c-peptide, and free fatty acid.

Figure 6. Showed the effect of resistant dextrin on the apoptosis parameters against the STZ induced GDM in rats. **a:** Bcl-2, **b:** caspase-3 and **c:** Bax. All the data showed as means ± standard error of the mean (SEM).



###Significant variation at $P < .001$
***Significant variation at $P < .001$

Visfatin and ICAM-1

GDM-induced rats were exposed to an increased level of ICAM-1 (Figure 3a) and visfatin (Figure 3b), and resistant dextrin significantly ($P < .001$) restored the levels of ICAM-1 and visfatin, almost reaching normal levels.

Antioxidant parameters

GDM rats significantly ($P < .001$) displayed improved levels of MDA (Figure 4a) and suppressed levels of SOD (Figure 4b), CAT (Figure 4c), GPx (Figure 4d), and GST (Figure 4e). Treatment of GDM rats with resistant dextrin significantly ($P < .001$) modulated the levels of antioxidant parameters.

Inflammatory cytokines and parameters

GDM group rats exhibited altered levels of TNF-α (Figure 5a), IL-6 (Figure 5b), IFN-γ (Figure 5c), IL-2 (Figure 5d), IL-4 (Figure 5e), and IL-10 (Figure 5f). Resistant dextrin treatment significantly ($P < .001$) restored the levels of inflammatory cytokines.

Apoptosis parameters

GDM-induced group rats displayed the repressed level of Bcl-2 (Figure 6a), caspase-3 (Figure 6b) ,improved level of Bax (Figure 6c), and resistant dextrin significantly ($P < .001$) altered the level of apoptosis parameters.

mRNA expression

Figure 7 exhibited the effect of the resistant dextrin on the mRNA. GDM rats exhibited the significantly ($P < .001$) increased expression of TLR4 (Figure 7a), MyD88 (Figure 7b), NF-κBp65 (Figure 7c), NLRP3 (Figure 7d), and resistant dextrin significantly ($P < .001$) suppressed the mRNA.

Histopathology

GDM group rats hepatic histopathology exhibited mild to moderate hepatocyte steatosis, individual liver cells

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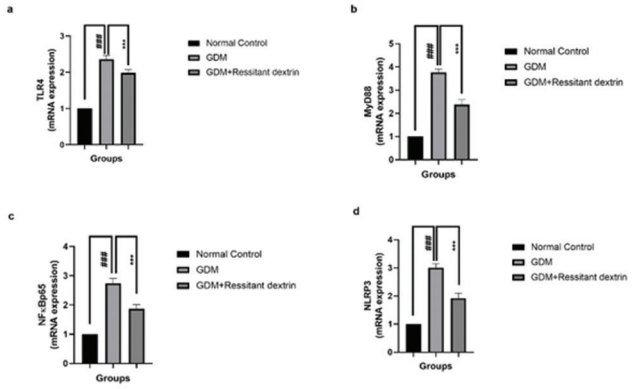
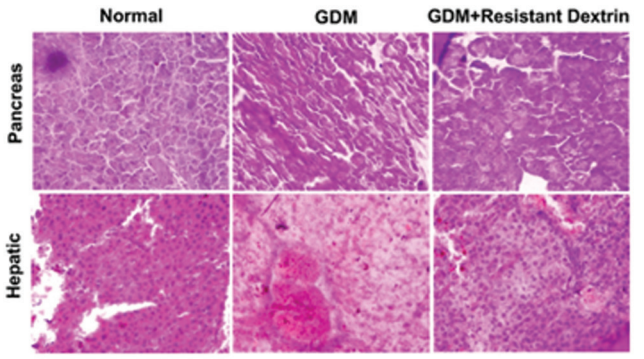
Figure 7. Showed the effect of resistant dextrin on mRNA expression against the STZ induced GDM in rats. **a:** TLR4, **b:** MyD88, **c:** NF-κBp65 and **d:** NLRP3. All the data showed as means ± standard error of the mean (SEM).



###Significant variation at $P < .001$
***Significant variation at $P < .001$

undergo necrosis and degeneration, and focal inflammatory cell infiltration, which was suppressed by the resistant dextrin. GDM-induced pancreas histopathology displayed the reduction of β-cells and pancreatic islets with the inflammatory cell infiltration and resistant dextrin altered the pancreatic histopathology changes (figure 8).

Figure 8. showed the effect of resistant dextrin on the pancreas and hepatic histopathology against the STZ induced GDM in rats.



DISCUSSION

STZ treatment of Langerhans pancreatic β cells resulted in apoptosis induction and the development of diabetes because the cells were unable to generate insulin at physiologically normal levels.[17,18] GDM can affect both maternal body weight and placenta weight during pregnancy.[4] The GDM is likely to suppress the weight during pregnancy compared to rats without GDM.[4] This is because the insulin resistance associated with GDM can cause more glucose to be stored as fat, leading to increased maternal adiposity. Additionally, a decrease in weight during pregnancy can further worsen insulin resistance and elevate the risk of developing type 2 diabetes later in life.[19] Because it provides the embryo with nutrition and oxygen, the placenta is essential to the growth and development of the fetus. But a larger placenta can also be a sign of placental malfunction, which could raise the risk of problems like fetal growth limitation and pre-eclampsia.[15]

Insulin resistance and impaired glucose metabolism are key features of GDM, and insulin therapy is often used to manage this condition. The cornerstone of GDM treatment is insulin therapy, which lowers the risk of problems for both the mother and the fetus while assisting in blood glucose management.[1,20] If diet and activity changes don't control blood sugar levels or if blood sugar levels don't go down despite these efforts, insulin therapy may be started. Insulin therapy is generally thought to be safe and does not increase the risk of birth abnormalities or other unfavorable outcomes for either the mother or the unborn child.[1,3,] In actuality, the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) is one method for assessing insulin resistance. It entails utilizing insulin and fasting blood glucose levels to calculate an index. Higher HOMA-IR values in the GDM setting indicate a higher degree of insulin resistance. Since GDM and the related metabolic alterations are largely caused by insulin resistance, this is an important parameter to keep an eye on. The HOMA-IR measure sheds light on how well insulin functions to maintain glucose homeostasis in pregnant women.[10,21,22]

Adipose tissue secretes the hormones adiponectin and leptin, essential for controlling insulin sensitivity and glucose metabolism. In the context of GDM, where there is impaired glucose metabolism and insulin resistance, both adiponectin and leptin may contribute to the development of this condition. Their involvement in the intricate network of hormonal regulation can influence the balance of glucose metabolism and insulin responsiveness during pregnancy, potentially influencing the onset or progression of GDM.[23] It is evident that adiponectin contributes to increased insulin sensitivity and better skeletal muscle and adipose tissue glucose absorption. Consequently, decreased adiponectin levels may factor in GDM's insulin resistance and poor glucose metabolism. Leptin, on the other hand, is involved in regulating energy balance and appetite. In the context of GDM, it may contribute to the development of the condition by promoting insulin resistance and impairing glucose metabolism. The intricate interplay of these hormones in the regulation of insulin sensitivity and glucose metabolism highlights their potential impact on the pathophysiology of GDM.[24] Rats with GDM had reduced levels of adiponectin and greater amounts of leptin. However, when the GDM group rats were treated with resistant dextrin, these hormonal levels were restored to normal.

ICAM-1 and Visfatin are two biomarkers that have been studied in relation to GDM.[25] ICAM-1, a molecule integral to the adhesion and migration of immune cells to inflammatory sites, exhibits elevated levels in gestational diabetes mellitus (GDM). This elevation implies a potential role for ICAM-1 in GDM development, possibly through the promotion of inflammation and insulin resistance. On the other hand, visfatin, an enzyme involved in the control of insulin

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sensitivity and glucose metabolism, may induce insulin resistance and hinder glucose metabolism, which could lead to the development of GDM.[15,25]

When pregnant women without a history of diabetes experience elevated blood glucose levels, it is known as GDM. Oxidative stress, or an imbalance between the body's antioxidant defense mechanisms and ROS production, has been linked to the development of GDM.[26,27] Antioxidant defense systems, comprising MDA, SOD, CAT, GSH, GPx, and GST, are pivotal in shielding against oxidative stress. MDA serves as a biomarker, indicating lipid peroxidation and, consequently, oxidative stress. Meanwhile, SOD, acting as an enzyme, is vital because it catalyzes the conversion of superoxide radicals into oxygen and hydrogen peroxide, which is a vital component of the body's defensive mechanism against free radical damage (Ma et al. 2022). The enzyme known as CAT reduces oxidative stress by catalyzing the breakdown of hydrogen peroxide into water and oxygen. By scavenging ROS, the tripeptide GSH is essential to the antioxidant defense system.[19,26] GPx is an enzyme that uses GSH as a cofactor to convert hydrogen peroxide and organic hydroperoxides to water and alcohol, respectively. The enzyme GST catalyzes the conjugation of GSH with electrophilic chemicals, which leads to their detoxification.[24,27] In the context of GDM, there were changes in the levels of antioxidant parameters. Notably, the introduction of resistant dextrin led to a significant modulation of these antioxidant parameters.

There is a correlation between inflammatory cytokines and markers and the advancement of GDM. Insulin resistance and hyperglycemia are facilitated by TNF-α and IL-6, which both lower glucose absorption in target tissues and disrupt insulin signaling.[15] Conversely, it has been noted that people with GDM have lower levels of anti-inflammatory cytokines such as IL-4 and IL-10. These cytokines can promote insulin sensitivity and glucose uptake in target tissues, improving glycemic control. Indeed, IL-2 is another cytokine implicated in the development of GDM. Research indicates that IL-2 levels are decreased during the GDM condition, suggesting a potential role for IL-2 in contributing to the development of insulin resistance.[23] INF-γ is a cytokine found to have a protective effect in GDM. IFN-γ may positively impact insulin sensitivity and glucose uptake in target tissues. This suggests that IFN-γ may play a part in lowering the chance of getting GDM.[28]

An anti-apoptotic protein called Bcl-2 contributes to preventing cell death. According to studies, Bcl-2 expression is downregulated in GDM patients, which may help target organs, including the placenta and adipose tissue, experiencing oxidative stress and apoptosis.[29] The reduction in Bcl-2 expression may contribute to the dysfunction of beta cells in the pancreas, resulting in impaired insulin secretion and glucose intolerance. Bax, a pro-apoptotic protein capable of promoting cell death, shows an opposite trend to Bcl-2. Studies have demonstrated an increase in Bax expression during GDM.[30] Increased expression of Bax could be a factor in the pancreatic beta cells' death, which would impede insulin output and induce glucose intolerance. Caspase-3 is a protease that is involved in the execution phase of apoptosis. Studies have shown that caspase-3 expression and activity increase during the GDM condition.[30.31] Elevated caspase-3 activity could be a factor in pancreatic β-cell death, which would result in reduced insulin production and glucose intolerance. Furthermore, an increase in caspase-3 activity could be a factor in placental cell death, which could result in placental malfunction and consequences such as fetal growth limitation and preeclampsia. Bcl-2, Bax and caspase-3 characteristics collectively contribute to the pathophysiology of GDM and its sequelae. Target tissues, including the pancreas and placenta, may become dysfunctional due to oxidative stress, apoptosis, and an imbalance between pro- and anti-apoptotic proteins.[31] Understanding the importance of these characteristics in GDM may open the door to the creation of innovative therapeutic approaches for the disease's treatment and prevention. Insulin resistance and the inflammatory response are strongly correlated in GDM. Tyrosine phosphorylation of IRS-1, an important signaling protein involved in insulin action, can be inhibited by inflammatory cytokines such as TNF-α, which can affect insulin signal transduction.[32]

Moreover, by triggering the NF-κB pathway, TLR4 activation can start the inflammatory response. The creation of pro-inflammatory cytokines, such as TNF-α, is the outcome of this activation.[15] TLR4-mediated activation of NF-κB, a critical transcription factor that controls the expression of several pro-inflammatory genes, is facilitated by the MyD88-dependent signaling pathway.[12]

CONCLUSION

Research indicates that resistant dextrin can mitigate insulin resistance and enhance glucose metabolism by influencing the gut microbiota and reducing inflammation. Resistant dextrin may reduce inflammation in GDM by blocking the TLR4/MyD88/NF-κB signaling cascade, among other possible methods. In target tissues, including skeletal muscle and adipose tissue, this inhibition may decrease the synthesis of pro-inflammatory cytokines and improve insulin sensitivity. Therefore, as a regulator of the inflammatory response and glucose metabolism in GDM, resistant dextrin has therapeutic potential.

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