绿原酸对高脂饲料诱导的肥胖大鼠糖耐量及其曲线特征的影响

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[摘 要] 目的:观察绿原酸(chlorogenic acid,CGA)对高脂饲料诱导的肥胖(diet-induced-obesity,DIO)大鼠糖耐量及其曲线特征的作用,为开发利用 CGA 早期预防和延缓糖尿病的发生提供依据。方法:46 只雄性 Sprague-Dawley (SD)大鼠随机选择 8 只作为普通饲料组(normal control group,CON),其余大鼠饲喂高脂饲料。4 周后按标准筛选高脂诱导的肥胖大鼠 24 只并随机分为高脂饲料组(high fat diet group,HFD)、50%(质量分数)CGA 组和 98%(质量分数)CGA 组,每组 8 只,分别给予磷酸缓冲盐溶液(phosphate buffer saline,PBS)、50% CGA 和 98% CGA 灌胃 8 周,每周检测体质量,每 4 周进行一次口服糖耐量试验(oral glucose tolerance test,OGTT),实验期末检测空腹胰岛素及胰岛素释放,计算稳态模型胰岛素抵抗指数(homeostasis model assessment insulin resistance,HOMA-IR)和内脏脂肪百分比,苏木精和伊红(hematoxylin and eosin,HE)染色检测胰腺组织病理变化。结果:CGA 干预前,与 CON 组相比,HFD 组 OGTT 第 120 分时(OGTT-120min)血糖值($P < 0.05$)和葡萄糖曲线下面积(area under curve-glucose, AUC-G)($P < 0.05$)均显著升高;干预 4 周后葡萄糖峰值时间延迟($P < 0.05$);干预 8 周 HOMA-IR 指数显著升高且 OGTT-0min、OGTT-30min、OGTT-60min、OGTT-120min 胰岛素水平和胰岛素曲线下面积(area under curve-insulin, AUC-I)显著升高($P < 0.05$),胰腺胰岛显著增生($P < 0.05$)。与 HFD 组相比,干预 4 周末,50% CGA 和 98% CGA 组大鼠糖耐量及其葡萄糖峰值时间均无显著变化;干预 8 周后,50% CGA 组大鼠 OGTT-60min、OGTT-120min 血糖值,HOMA-IR 指数,OGTT-0min、OGTT-30min、OGTT-120min 血清胰岛素水平显著降低($P < 0.05$);98% CGA 组大鼠 OGTT-60min、OGTT-120min 血糖值,HOMA-IR 指数,OGTT-0min、OGTT-120min 血清胰岛素水平显著降低($P < 0.05$);50% 和 98% CGA 组大鼠的葡萄糖峰值时间均显著前移($P < 0.05$),胰岛异常增生改善($P < 0.05$)。结论:OGTT 葡萄糖峰值时间延迟是 DIO 大鼠糖耐量异常表现之一,50% 和 98% CGA 均可改善 DIO 大鼠的糖耐量和葡萄糖峰值时间延迟。

[关键词] 绿原酸;肥胖;糖耐量异常;OGTT 葡萄糖峰值时间

Effects of chlorogenic acid on glucose tolerance and its curve characteristics in high-fat diet-induced obesity rats

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ABSTRACT Objective:To observe the effect of chlorogenic acid (chlorogenic acid, CGA) on the glucose tolerance and its curve characteristics in high fat diet-induced obesity (diet-induced-obesity, DIO) rats, so as to provide scientific grounds for the development and utilization of CGA in early prevention and reversal of prediabetes. Methods:Eight of forty-six male Sprague-Dawley rats were randomly selected as the normal diet group (CON group), and the rest were fed with high-fat diet. After 4 weeks, 24 high-fat-induced obese rats were screened according to the criteria and then randomly divided into high fat diet group (HFD group), 50% CGA group and 98% CGA group. The CGA groups received intragastric administrations of 50% CGA and 98% CGA orally via a gavage needle once a day for 8 weeks, respectively, while the CON and HFD groups received a carrier solution (phosphate buffer saline, PBS). Their body weights were measured weekly and oral glucose tolerance test (OGTT) was performed every 4 weeks. Fasting insulin and insulin release were measured at the end of the study. Meanwhile, HOMA-IR and visceral fat percentage were calculated. Histopathological examination by hematoxylin and eosin staining method were evaluated in the pancreatic tissues. Results:Before the intervention of chlorogenic acid, blood glucose levels 120 min after glucose loading ($P < 0.05$) and AUC-G ($P < 0.05$) were in-

creased in the HFD group when compared with the CON group, and the time to glucose peak was delayed after 4 weeks of chlorogenic acid intervention ($P < 0.05$). After 8 weeks of intervention, the HOMA-IR index, the insulin levels at 0 min, 30 min, 60 min, and 120 min after glucose loading and AUC-I increased ($P < 0.05$), and the histopathological examination showed obvious hyperplasia of pancreatic islets ($P < 0.05$). Compared with the HFD group, there was no significant change in glucose tolerance and glucose peak time in 50% CGA and 98% CGA groups at the end of 4 weeks of intervention. However, after 8 weeks of intervention, OGTT-60min, OGTT-120min blood glucose ($P < 0.05$) were lower, HOMA-IR index and OGTT-0min, OGTT-120min serum insulin level decreased ($P < 0.05$), the time to glucose peak shifted to an earlier timepoint ($P < 0.05$), abnormal islet hyperplasia attenuated ($P < 0.05$) in 50% CGA and 98% CGA groups. Also, the OGTT-30min serum insulin level was decreased ($P < 0.05$) in 50% CGA group. **Conclusion**: Delay in time to glucose peak during the OGTT was one of the manifestations of impaired glucose tolerance in DIO rats, and 50% and 98% CGA could improve the glucose tolerance and delay in glucose peak time.

KEY WORDS　Chlorogenic acid; Obesity; Impaired glucose tolerance; Oral glucose tolerance test glucose peak time

目前,糖尿病已成为世界好发性疾病,中国成年人糖尿病患病率为 10.9% ,糖尿病前期患病率为 35.7%[1],如不干预,进一步发展为糖尿病的风险高达 89.9% ,并增加心血管患病率与全因死亡率[2]。糖尿病前期包括空腹血糖受损(impaired fasting glucose,IFG)和糖耐量异常(impaired glucose tolerance,IGT)。IGT 比 IFG 能更灵敏地反映糖尿病前期糖代谢紊乱状况,目前临床通过检测 2 h 糖耐量筛查 IGT,约 40% 的 2 型糖尿病(type 2 diabetes mellitus,T2DM)患者在基线时 2 h 糖耐量正常[3]。流行病学研究表明,与空腹血糖和餐后两小时血糖相比,口服糖耐量试验(oral glucose tolerance test,OGTT)曲线特征可能会更好地预测未来发生糖尿病的风险。OGTT 曲线的葡萄糖峰值时间和峰值大小[4]、曲线形状[5]、OGTT 第 120 分时(OGTT-120min)血糖与空腹血糖之间的关系[6]和胰岛素浓度模式[7]包含了多种代谢相关信息,这些特征与糖耐量、胰岛素敏感性、胰腺 β 细胞功能和 T2DM 的发病风险相关,OGTT 曲线的葡萄糖峰值时间的稳定性最好[8]。在健康人群和 T2DM 患者中,葡萄糖峰值时间延迟(> OGTT-30min)提示胰岛素敏感性[4]和分泌降低[9],是 IGT 和 β 细胞功能下降的独立预测指标[10-12]。IGT 是 T2DM 发生和发展过程中的可逆阶段,早期识别和积极的生活方式干预可以成功地延缓或预防 T2DM 的进展[13]。因此,寻找可以有效防治 IGT 的方法对糖尿病防治具有重要的意义。

绿原酸(chlorogenic acid,CGA)是一种多酚类化合物,由肉桂酸和奎尼酸形成的酯,最常见的形式是 5-咖啡酰奎宁酸(5-CQA),广泛存在于植物和食物中,特别是金银花、杜仲、咖啡中富含 CGA。研究显示,CGA(生咖啡豆提取物)可以降低肥胖 IGT 患者的体质量、空腹血糖和胰岛素分泌,增加胰岛素敏感性[14]。CGA 还可改善肥胖 C57BL/6 小鼠高胰岛素血症和胰岛素抵抗指数[15],降低 db/db 小鼠糖尿病晚期口服糖耐量 15 min 时的葡萄糖峰值[16]。含 CGA 的咖啡提取物对大鼠糖耐量曲线下面积也有一定的改善作用[17]。本研究旨在采用金银花来源的不同纯度的 CGA,通过高脂饮食诱导建立肥胖大鼠(diet-induced-obesity, DIO)模型,探讨 CGA 对 DIO 大鼠糖耐量及其曲线特征变化的影响,为开发利用 CGA 早期预防或延缓糖尿病发生提供依据。

1　材料与方法

1.1　DIO 大鼠模型的建立

46 只 SPF 级 5 周龄雄性 Sprague-Dawley（SD）大鼠,体质量 140 ~ 160 g(购自北京维通利华有限公司,实验动物生产许可证号:SCXK(京)2016-0010,使用许可证号:SYXK(京)2016-0041)。饲养在 SPF 级环境中,恒温恒湿[温度(25 ± 2) ℃ ,湿度 55% ± 10%], 12 h 光照-黑暗循环,自由采食饮水。适应性喂养 1 周后, 按体质量区组化随机分组法分为普通饲料组(CON 组,$n = 8$)和高脂饲料组($n = 38$), 2 只/笼。CON 组给予能量密度为 3.49 kcal/g(供能比:脂肪 13% 、蛋白质 27% 、碳水化合物 60%)的普通饲料(购自北京科澳协力饲料有限公司);高脂饲料组给予能量密度为 4.73 kcal/g(供能比:脂肪 45% 、蛋白质 20% 、碳水化合物 35%)的高脂饲料(购自 Research Diets,D12541)。高脂组大鼠自由采食,CON 组根据高脂组大鼠进食量高值定量给予普通饲料。喂养 4 周后,高脂组大鼠依据体质量高于 CON 组体质量均值[体质量(397.2 ± 57.2) g]10% 的标准[18]筛选出 DIO 大鼠[体质量(465.3 ± 37.3) g]24 只。

本研究开始前已经北京大学生物医学伦理委员会动物伦理分会审查批准(LA2017002)。

1.2　实验分组与处理

将 24 只 DIO 大鼠随机分为高脂饲料组(HFD 组,$n = 8$)、50%(质量分数)绿原酸组(50% CGA 组,$n = 8$)和 98%(质量分数)绿原酸组(98% CGA 组,$n = 8$),持续高脂饲料喂养;CON 组持续普通饲料喂养。CGA 组分别灌胃给予 50% 和 98% CGA 的溶液(金银花提取物,购自山东禾本堂生物科技有限公司),剂量 80 mg/kg,用 0.1 mol/L 的磷酸缓冲盐溶液(phosphate buffer saline,PBS)配制为浓度 30 g/L,现配现用,1 次/d,共 8 周。CON 组和 HFD 组均给予等量的 PBS(pH = 7.4)。

1.3 观察指标与方法

1.3.1 体质量和体脂肪 实验期间每周称体质量和进食量。CGA 干预 8 周末,大鼠禁食过夜,称质量后经 2%(质量分数)戊巴比妥纳(0.3 mL 每 100 g)腹腔注射麻醉,测体长(鼻尖至肛门的距离),计算 Lee's 指数[Lee's 指数 = $\sqrt[3]{\text{体质量(g)} \times 1\,000/\text{体长(cm)}}$]。大鼠处死后剥离肾周及附睾脂肪组织,称质量,计算内脏脂肪百分比[(双侧肾周脂肪质量 + 附睾脂肪质量)/体质量 ×100%]。

1.3.2 糖耐量及稳态模型胰岛素抵抗指数 在 CGA 干预前、干预 4 周末、干预 8 周末进行 OGTT。大鼠禁食过夜,灌胃给予 50% 葡萄糖溶液(2 g/kg),剪尾采血,血糖仪(ACCU-CHEK Advantage,Roche,DE)测定 OGTT-0min、OGTT-15min、OGTT-30min、OGTT-60min 和 OGTT-120min 的血糖,根据梯形公式计算葡萄糖曲线下面积(area under curve-glucose,AUC-G)[19];同时对大鼠进行眼内眦取血,ELISA 法(Millipore,EZRMI-13K)检测 OGTT-0min、OGTT-30min、OGTT-60min 及 OGTT-120min 血清胰岛素,并计算胰岛素曲线下面积(area under curve-insulin,AUC-I)和稳态模型胰岛素抵抗指数(homeostasis model assessment insulin resistance,HOMA-IR),HOMA-IR = FBG(mmol/L)× FINS(μU/L)/22.5(FBG:fasting blood glucose,空腹血糖;FINS:fasting insulin,空腹胰岛素)。

1.3.3 OGTT 葡萄糖曲线的形状特征 葡萄糖峰值时间是 OGTT 葡萄糖曲线特征之一,与不同代谢风险和 T2DM 的未来风险有关,其定义为 OGTT 曲线上出现的第一个波峰的时间点(OGTT-15min、OGTT-30min、OGTT-60min、OGTT-90min 或 OGTT-120min),其中葡萄糖波动阈值设为 0.25 mmol/L(4.5 mg/dL),避免由于实验不精确而导致的错误分类[20]。糖耐量正常人群中,多数在 OGTT-30min 内血糖达到最大值[9],且研究显示,正常大鼠的葡萄糖峰值时间一般在 OGTT-30min 之前[21],因此本

研究把血糖峰值时间分 ≤ OGTT-30min 和 > OGTT-30min 两类。

1.3.4 胰腺病理检查 CGA 干预 8 周末,2%(质量分数)戊巴比妥麻醉处死大鼠后取胰腺组织用甲醛固定,制备胰腺石蜡切片,HE 染色,在光学显微镜下计数每个样本 10 个 10 倍视野内的胰岛数目,并拍照。

1.4 统计学分析

采用 SPSS25.0 软件,正态分布的计量资料以 $\bar{x} \pm s$ 表示,两组(CON 组与 HFD 组)间比较采用独立样本 t 检验,多组(HFD 组、50% CGA 组和 98% CGA 组)间比较采用单因素方差分析;非正态分布的计量资料以中位数(最小值,最大值)表示,两组(CON 组与 HFD 组)间比较采用独立样本 Mann-Whitney U 秩和检验,多组(HFD 组、50% CGA 组和 98% CGA 组)间比较采用 Kruskal-Wallis 检验。分类计数资料采用卡方检验(Fisher 精确检验),$P < 0.05$ 认为差异具有统计学意义。

2 结果

2.1 CGA 对 DIO 大鼠体质量、体脂肪的影响

CGA 干预 8 周末,HFD 组大鼠体质量($t = -7.222, P < 0.001$)、Lee's 指数($t = -7.433, P < 0.001$)和内脏脂肪百分比($t = -10.154, P < 0.001$)均显著高于 CON 组(表 1)。与 HFD 组相比,50% CGA 组和 98% CGA 组大鼠的体质量($F = 0.388, P = 1.000, P = 1.000$)、Lee's 指数($F = 0.501, P = 1.000, P = 1.000$)和内脏脂肪百分比($F = 1.885, P = 1.000, P = 0.298$)均降低,但差异无统计学意义(表 1)。两个 CGA 组间大鼠体质量、内脏脂肪百分比和 Lee's 指数差异均无统计学意义。

表 1 CGA 对 DIO 大鼠体质量、Lee's 指数和内脏脂肪百分比的影响($\bar{x} \pm s$)

Table 1 Effects of CGA on body weight Lee's index and visceral fat percentage in DIO rats($\bar{x} \pm s$)

Items	n	Body weight/g	Lee's index	Visceral fat percentage/%
CON	8	498.9 ± 29.3	26.9 ± 0.5	3.0 ± 0.4
HFD	8	674.4 ± 62.2*	29.1 ± 0.7*	9.0 ± 1.6*
50% CGA	8	649.1 ± 50.3	28.8 ± 0.6	8.9 ± 2.6
98% CGA	8	655.0 ± 66.3	29.1 ± 0.8	7.2 ± 2.0

CON, normal control group; HFD, high fat diet group; CGA, chlorogenic acid. * $P < 0.05$, compared with the CON group.

2.2 CGA 对 DIO 大鼠糖耐量的影响(图 1)

与 CON 组相比,CGA 干预前,HFD 组大鼠 OG-TT-120min 血糖($t = -4.046, P = 0.001$)和 AUC-G($t = -2.979, P = 0.010$)升高(图 1A、1D),干预 4 周末 OGTT-60min($t = -4.426, P = 0.001$)、OGTT-120min 血糖($t = -5.138, P < 0.001$)和 AUC-G($t = -4.969, P < 0.001$)均升高(图 1B、1E)。干预 8 周末 OGTT-60min($t = -4.606, P < 0.001$)、OGTT-120min 血糖($t = -4.412, P = 0.001$)和 AUC-G($t = -3.090, P = 0.008$)均升高(表 2,图 1C、1F),OG-TT-15min 血糖($t = 5.201, P < 0.001$)显著降低,OG-TT-0min 血糖无明显变化。与 HFD 组相比,CGA 干预 4 周末,50% CGA 和 98% CGA 组大鼠 OGTT-60min、OGTT-120min 血糖和 AUC-G 均无明显变化(图 1B、1E);干预 8 周末,50% CGA 和 98% CGA 组的 OGTT-60min($F = 8.526, P = 0.007, P = 0.004$)和 OGTT-120min($F = 5.379, P = 0.020, P = 0.046$)血糖值降低,AUC-G 均无显著变化($F = 3.237, P = 0.094, P = 0.149$,表 2,图 1C、1F);此外,50% CGA 和 98% CGA 组之间 OGTT 各时间点血糖和 AUC-G 差异均无统计学意义($P > 0.05$,图 1)。
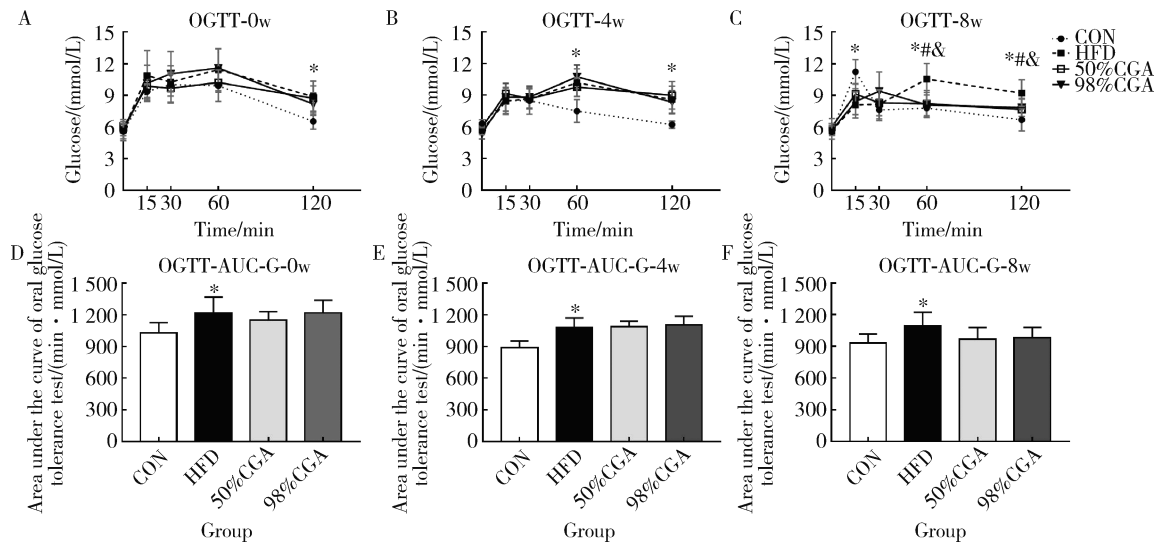
$n = 8$. CON, normal control group; HFD, high fat diet group; CGA, chlorogenic acid; AUC-G, area under curve-glucose; OGTT, oral glucose tolerance test. A to F, changes in the AUC-G and the OGTT curve of DIO rats before CGA intervention and after CGA intervention at 4 and 8 weeks. $*$ $P <$ 0.05, compared with the CON group; # $P < 0.05$, 50% CGA group compared with the HFD group; & $P < 0.05$, 98% CGA group compared with the HFD group.

图 1 CGA 对 DIO 大鼠糖耐量的影响
Figure 1 Effect of CGA on glucose tolerance in DIO rats

2.3 CGA 对 DIO 大鼠 OGTT 葡萄糖峰值时间的影响

CGA 干预 4 周末,与 CON 组(≤30 min,8 只; >30 min,0 只)相比,HFD 组大鼠 OGTT 葡萄糖峰值时间(≤30 min,3 只; >30 min,5 只)显著延迟(Fisher 精确检验,$P = 0.026$,图 1B)。与 HFD 组相比,干预 4 周末,50% CGA 和 98% CGA 组大鼠葡萄糖峰值时间(两组均为:≤30 min,3 只; >30 min,5 只)均无显著变化(Fisher 精确检验,$P = 1.000, P = 1.000$,图 1B)。CGA 干预 8 周末,与 CON 组(≤30 min,8 只; >30 min,0 只)相比,HFD 组大鼠 OGTT 葡萄糖峰值时间(≤30 min,2 只; >30 min,6 只)显著延迟(Fisher 精确检验,$P = 0.007$,图 1C),50% CGA 组大鼠葡萄糖峰值时间(≤30 min,8 只; >30 min,0 只)显著前移(Fisher 精确检验,$P = 0.007$,图 1C);98% CGA 组大鼠葡萄糖峰值时间(≤30 min,7 只; >30 min,1 只)显著前移(Fisher 精确检验,$P = 0.041$,图 1C)。两个 CGA 组间大鼠葡萄糖峰值时间间差异无统计学意义(Fisher 精确检验,$P = 1.000$,图 1C)。

2.4 CGA 对 DIO 大鼠的血清胰岛素水平和 HOMA-IR 的影响

CGA 干预 8 周末,与 CON 组相比,HFD 组 DIO 大鼠 OGTT-0min、OGTT-30min、OGTT-60min 和 OG-TT-120min 的血清胰岛素均显著升高($t = -3.903, P = 0.003; t = -3.369, P = 0.007; t = -2.799, P < 0.019; t = -6.077, P < 0.000$,图 2A),同时 AUC-I 升高($t = -4.967, P = 0.001$,图 2B),HOMA-IR 也升高[8.15(1.82, 19.39) $vs.$ 24.29(16.95, 34.36),$z = -2.562, P = 0.010$]。与 HFD 组相比,50% CGA 组 OGTT-0min、OGTT-30min、OGTT-120min 的血清胰岛素水平($F = 9.928, P = 0.015; F = 5.159, P = 0.044; F = 5.050, P = 0.041$)显著降低(图 2A);HOMA-IR 也显著降低[24.29(16.95, 34.36) $vs.$ 11.63(5.67,14.66),$P = 0.031$];AUC-I

降低,但差异无统计学意义($F = 2.923, P = 0.198$,图 2B);98% CGA 组大鼠 OGTT-0min($F = 9.928$, $P = 0.004$)、OGTT-120min($F = 5.050, P = 0.047$)的血清胰岛素水平显著降低(图 2A),OGTT-30min

($F = 5.159, P = 0.058$)的血清胰岛素水平和 AUC-I($F = 2.923, P = 0.163$,图 2B)降低,但差异无统计学意义;HOMA-IR 显著降低[24.29(16.95,34.36) $vs.$ 5.66(3.89,24.41),$P = 0.004$]。
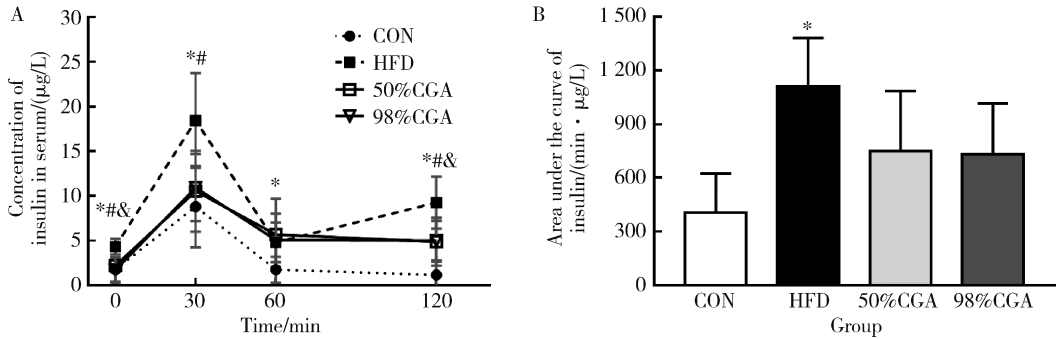
$n = 6$. A,insulin release test of DIO rats;B,area under curve-insulin,AUC-I. ＊$P < 0.05$,CON group compared with the HFD group;# $P < 0.05$, 50% CGA group compared with HFD group;& $P < 0.05$, 98% CGA group compared with HFD group.

图 2　CGA 对 DIO 大鼠 OGTT 胰岛素分泌的影响

Figure 2　Effect of CGA on insulin secretion of OGTT in DIO rats
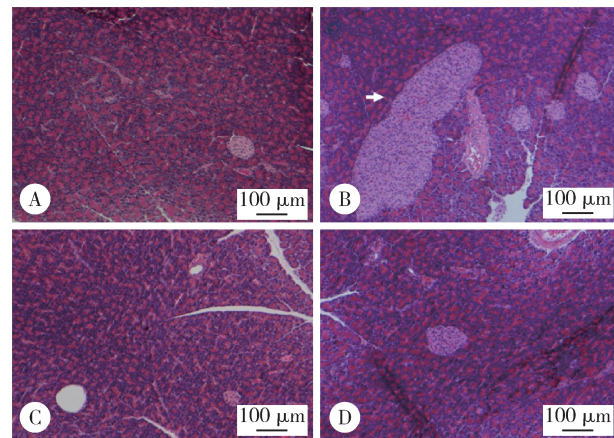
2.5　CGA 对 DIO 大鼠胰腺胰岛的影响

胰腺病理结果显示,CGA 干预 8 周末,与 CON 组[14(2,18)]相比,HFD 组胰腺可见胰岛数目增多[18(14,26),$z = -2.857, P = 0.004$]、大小不一、形态不规整(图 3A 和 3B);与 HFD 组大鼠相比,50% CGA[15(8,22),$P = 0.032$]和 98% CGA[11(4,22),$P = 0.004$]胰岛数目异常增多减轻(图 3C 和 3D),两个 CGA 组间胰岛数目差异无统计学意义。

A,CON group;B,HFD group;C,50% CGA group;D,98% CGA group. Scale bars = 100 μm. White arrow:abnormally enlarged islet.

图 3　DIO 大鼠胰腺病理学变化(HE ×100)

Figure 3　Pathological changes of pancreas in DIO rats(HE ×100)

3　讨论

本研究高脂饲料喂养 4 周后,DIO 大鼠 OGTT-120min 血糖和 AUC-G 升高,12 周后糖耐量异常加重,OGTT 葡萄糖峰值时间延迟(> OGTT-30min),胰岛异常增生,血清胰岛素水平升高,出现胰岛素抵抗,分别给予 50% CGA 和 98% CGA 干预 8 周,可以降低 DIO 大鼠 OGTT-60min、OGTT-120min 的血糖值,改善葡萄糖峰值时间。

本研究 3 组 DIO 大鼠的进食量差异无统计学意义(数据未显示),说明 CGA 可能不会抑制 DIO 大鼠的食物摄入。给予 CGA 8 周后,DIO 大鼠的体质量和内脏脂肪百分比有所下降,50% CGA 组内脏脂肪百分比下降1.1%,98% CGA 组下降20.2%,表明 98% CGA 对内脏脂肪有一定的改善作用。

CGA 干预前,HFD 组 DIO 大鼠 OGTT-120min 血糖和 AUC-G 升高,表明 SD 大鼠摄入脂肪供能比为45%的高脂饲料 4 ~ 5 周后可表现出糖耐量异常。继续高脂饲料喂养 8 周,HFD 组大鼠的胰岛代偿性增生,OGTT-0min、OGTT-30min、OGTT-60min 和 OGTT-120min 血清胰岛素均升高,而 OGTT-120min、OGTT-60min 血糖和 AUC-G 仍处于升高水平,表明 DIO 大鼠出现胰岛素抵抗。此外,与 CON 组相比,HFD 组大鼠空腹血糖未出现明显变化,表明相较于 IGT,用 FPG 筛查糖尿病的敏感性较低[22]。给予 50% 和 98% CGA 干预 8 周后,DIO 大鼠的 OGTT-60min、OGTT-120min 血糖和 HOMA-IR 降低,胰岛增生减弱,提示 CGA 可以改善 DIO 大鼠糖耐量可能与 CGA 抑制胰岛增生,改善高胰岛素血症和胰岛素抵抗有关。98% CGA 主要是单一成分 CGA,而 50% CGA 只有一半 CGA,50% CGA 改善 DIO 大鼠糖耐量除了 CGA 作用,可能也与其他生物活性成分有关,这尚待进一步研究。

葡萄糖峰值时间 > OGTT-30min 时间点是糖尿

病前期和 β 细胞功能降低的独立指标。本研究发现,CGA 可以改善 DIO 大鼠 OGTT 葡萄糖峰值时间。在高脂饲料喂养 8 周末, HFD 组 DIO 大鼠出现葡萄糖峰值时间延迟(> OGTT-30min),并持续到实验终止,伴随 AUC-G、血清胰岛素和 HOMA-IR 的升高,表明葡萄糖峰值时间 > OGTT-30min 时间点与 OGTT 期间较差的代谢特征相关。50% 和 98% CGA 干预 4 周对葡萄糖峰值未见影响,干预 8 周后可以显著改善葡萄糖峰值时间的延迟,与 OGTT 期间的其他代谢参数得到改善的结果一致,提示两种纯度的 CGA 均可改善高脂诱导的糖耐量异常曲线特征,保护 β 细胞功能。有关 CGA 改善葡萄糖峰值时间延迟的机制有待进一步研究。

综上所述,本研究发现两种不同浓度的 CGA (金银花提取物)可以改善高脂饲料诱导的 SD 大鼠糖耐量异常和 OGTT 曲线葡萄糖峰值时间延迟,对开发利用金银花提取物早期预防和延缓糖尿病的发生可能具有重要意义。

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