

**Judiono . Plain Kefir Antidiabetic Potential: Study on glyceimic, antioxidants status, immune response and pancreatic  $\beta$  cell regeneration on hyperglycemia Wistar rats Streptozotocin induced.**

**Abstract.**

*Background.* Oxidative stress triggers the function and structure of pancreatic  $\beta$  cell damage in hyperglycemia through lipid peroxidation, proinflammatory cytokines modulation and interleukin-10. The available therapy so far has not been reaching an optimal of the blood glucose control. Kefir's bioactive have potential as a supplement therapy. This study was aimed at validating the effect of plain kefir on glyceimic, antioxidants status, immune response and pancreatic  $\beta$  cell regeneration of hyperglycemia Wistar Strain Rats induced by Streptozotocin (STZ).

*Materials and Method.* The randomized pretest - posttest control group study design was conducted in male hyperglycemia Wistar rats induced by 40 mg / kg body weight streptozotocin (STZ) dissolved in 0,1 M buffer citrate pH 4,5. Rats were randomized into four groups, namely: (1) STZ-induced animals group and given insulin treatment UI/200 0.76 g bw, (2) STZ-induced animals group and given treatment plain kefir 3.6 cc/200 g bw/day for 30 days, (3) STZ-induced animals group (non-STZ induced) as a positive control (ad libitum), (4) normal animals group as a negative control (ad libitum). Blood glucose was measured by enzymatic method. Antioxidants status (SOD, GPX) were measured by ELISA. Catalase was measured by Spectrofometry. Lipid peroxide was measured MDA-TBARs by spectrofotometry. Immune response (cytokines IL<sub>1</sub>, IL<sub>6</sub>, TNF <sub>$\alpha$</sub> , IL<sub>10</sub>) were measured by ELISA. Pancreatic histology was observed by immunohistochemistry. Data were analyzed by One Way Anova, Mann Whitney test, Duncan, Ancova with significance level  $p < 0.05$ .

*Result.* Plain kefir supplementation 3.6 cc / day affect significantly on blood glucose, antioxidants (SOD, Catalase, GPX), lipid peroxidation (MDA), and pancreatic  $\beta$ -cells regeneration. Statistical analysis showed respectively decrease of glucose ( $p < 0.001$ ), MDA ( $p < 0.001$ ), level of proinflammatory cytokines (IL<sub>1</sub>, IL<sub>6</sub>) ( $p < 0.001$ ), except of controls. Antioxidant capacity showed increase of catalase, GPx ( $p < 0.001$ ) and SOD ( $p < 0.05$ ). Similarly, there was increased of IL<sub>10</sub> ( $p < 0.05$ ) and the normal cells pancreatic  $\beta$  expression ( $p < 0.001$ ), except of control. TNF $\alpha$  was reduced. Ancova test showed MDA and IL<sub>10</sub> were the most contributed to the pancreatic  $\beta$  cells regeneration by 91.0% and 9% determined by TNF- $\alpha$ , antioxidants, blood glucose, body weight. Probiotics kefir were found in as many as  $10^6$ - $10^9$  cfu / mL and declined to  $10^5$  as the decrease in pH during storage.

*Conclusion and recommendation.* Kefir supplementation about 3.6 cc/ day has significantly decreased (1) blood glucose, (2) lipid peroxide (MDA),(3) level of cytokines ( IL<sub>1</sub>, IL<sub>6</sub>) and (4) enhanced IL<sub>10</sub> and (5) antioxidants capacity (SOD, Catalase, GPx) and (6) normal pancreatic  $\beta$  cell expression. Insulin and kefir descriptively reduced TNF  $\alpha$  level. It is necessary to disclose underlying biomolecular mechanism and characterization of plain kefir probiotics before applying clinically to diabetic patients.

*Keyword:* Probiotic, plain kefir, diabetes mellitus, hyperglycemia, free radicals,  $\beta$  cells regeneration, proinflammatory cytokines