Role of Probiotics and Anti-glycative Compound in Prevention of Diabetic Nephropathy

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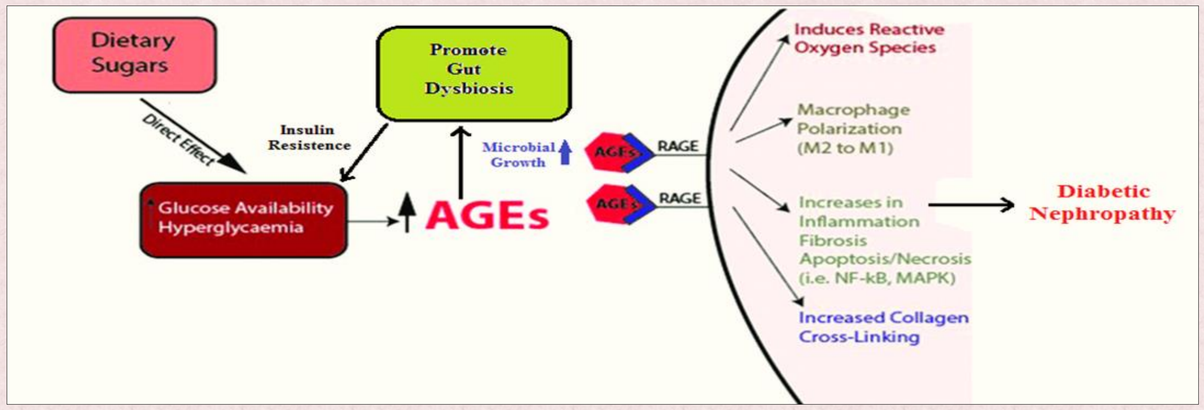
ABSTRACT

Hyperglycemia has an important role in the pathogenesis of diabetic complications by increasing protein glycation and further accumulation of advanced glycation end products (AGEs) in body. AGEs are accompanied by increased free radical activity that contributes to bimolecular damage in diabetes. It is evidenced that interaction of AGEs with RAGE alters, gene expression, by increase in various pro-inflammatory cytokines and free radicals that contribute towards the pathobiology of diabetic complications. There is considerable role of anti-glycation compounds (AGC) because of their therapeutic potential. There is also evidence that AGEs can promote gut microbial growth which leads to gut dysbiosis which results into gut permeability. Studies have shown that probiotics can repair gut barrier and hence it may increase insulin sensitivity and helps in controlling glycemic index in body. Consequently, we hypothesize that probiotics and AGC help in maintaining blood glucose level and hence may prevent AGEs formation, which can further prevent the diabetic nephropathy (DN).

INTRODUCTION

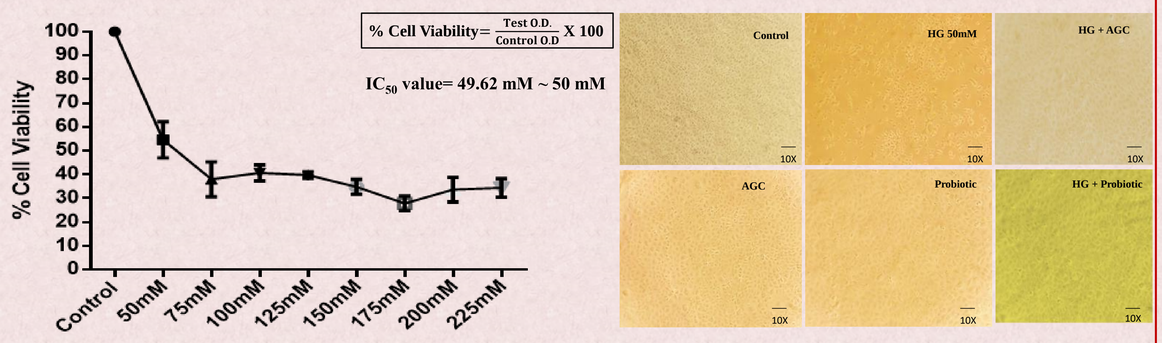
Around 25–40% of type 1 or type 2 diabetic patients develop diabetic nephropathy after 20 years of the onset of diabetes. Diabetic complication is associated with glycation which non-enzymatically modifies proteins, nucleic acids and lipids due to hyperglycemic condition forming Schiff bases, Amadori products and finally result in formation of AGEs via a process called as Maillard reaction. AGEs interacts with its receptor RAGE, induce oxidative stress and activate MAPK pathway which result in increase in expression of proinflammatory cytokines. Vlassara *et al* (2014) had reported that AGEs are responsible in damage of islet of β cells and impairing insulin secretion by generation of ROS which suppress deacetylase SIRT1 whose role is to decrease inflammation, apoptosis and mitochondrial biogenesis by inhibiting UCP2 involved in insulin secretion. It is evidenced that AGEs promote growth of gut microbiota which leads to gut dysbiosis and results in increase in gut permeability. Hence endotoxins produced by gram negative bacteria enter the liver through gut-liver axis which upon binding with its receptor TLR4,results in increase in proinflammatory genes like IL-6, MCP-1 etc. This inflammatory response lead to reduce insulin stimulated IRS-1,Akt phosphorylation and impairs glucose transport.



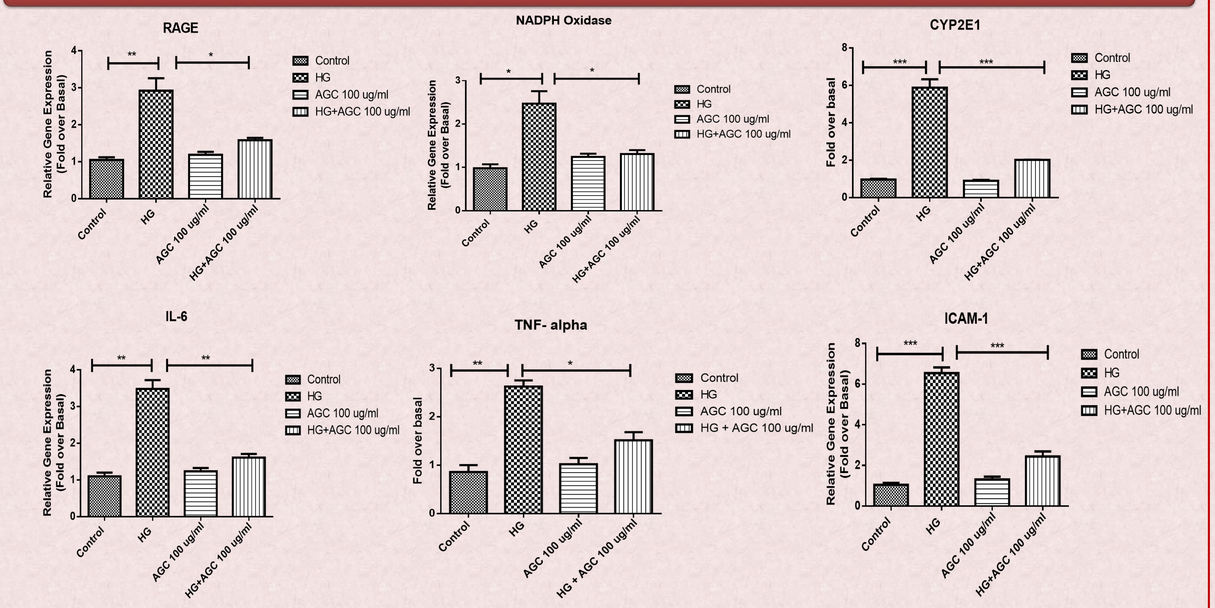
Materials and Methods

Normal Rat Kidney (NRK-52E) cells were procured from National Centre for Cell Sciences, Pune and were maintained at 37°C with 5% CO_2 in Dulbecco's Modified Eagle's Medium with 10% Fetal Bovine Serum and 1% antibiotic-antimycotic solution. Glucose toxicity was checked using MTT assay and the dose of glucose was determined thereof. Further, $8x10^5$ NRK-52E cells were seeded on Day1. After 24 h, cells were treated with 50 mM high glucose (HG) in presence and absence of 100 µg/ml antiglycative compound (AGC) and 10µl probiotic cell free supernatant. RNA isolation was done after 24 h of treatment and expressions of different genes were analyzed by qRT-PCR.

RESULTS

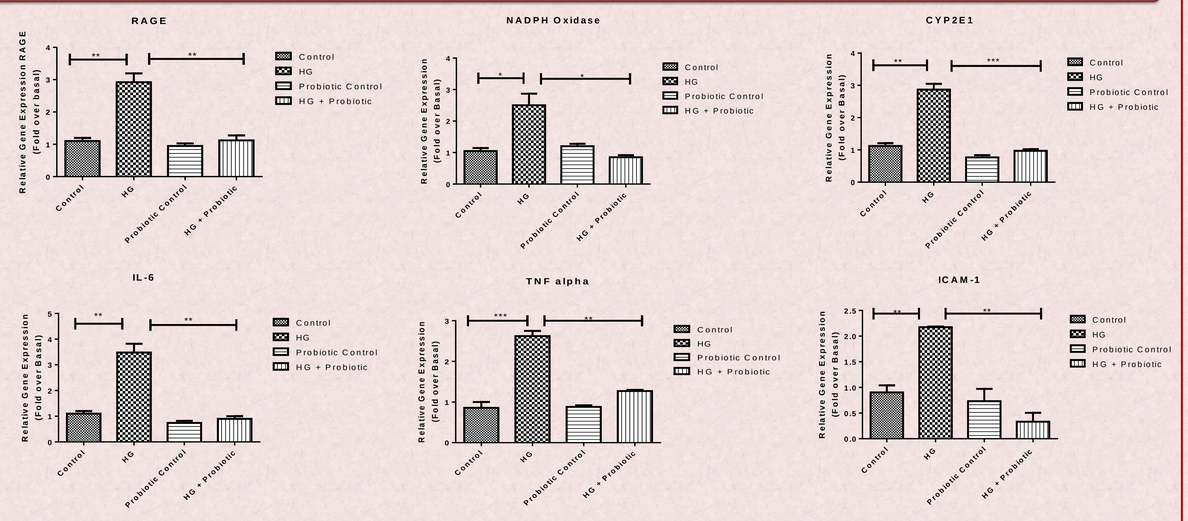


Effect of AGC on various genes in the presence of HG



Results are means ± SEM of three different experiments. *p < 0.05, **< 0.01, ***<0.001, ****<0.0001

Effect of probiotics on various genes in the presence of HG



Results are means ± SEM of three different experiments. *p < 0.05, **< 0.01, ***<0.001, ****<0.0001

Conclusion

Current study identifies that probiotics and AGC reduce harmful effects of high glucose by down-regulating the inflammation and oxidative stress. AGC may inhibit AGEs formation and can prevent progression of diabetic nephropathy. Additionally, probiotics might prevent formation of AGEs by balancing the glucose level.

References

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Acknowledgement

Authors would like to be thankful to Charotar University of Science and Technology for providing the CPSF and the facilities to carry out the research work.

Presented at National level virtual symposium on Recent Trends in Modern Biology at CHARUSAT, Changa, Gujarat, India 10-12 December, 2020