How microbiome affects glycemic excursions?

HI!

I am Dr. Mahpara Safdar

I am here because I love to interact with people who are eager to learn, communicate and share.

I can be reached at mahpara.jadoon@aiou.edu.pk

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Gut Microbiome and;

- Its structure and functions
- Type 1 diabetes
- Type 2 diabetes
- Medications
- Eating habits and lifestyle factors

“If you get the inside right, the outside will fall into place”

ECKHART TOLLE

Microbiome, its structure and function

Microbiome , its structure and function

- The human gut harbors **diverse microbes** that play a fundamental role in the well-being of their host.
- Each body has a unique array of these microorganisms, collectively called the **'microbiota:**.
- The most abundant population of these microorganisms present in the **gut**
- Reaching **trillions of cells per gram** in the distal colon
- Biomass within the gut may reach up to **1.5 kg, over 1000 different species** of bacteria

Microbiome , its structure and function

- Over 100-fold more genes than are in the human genome
- **Symbiotic relationship** between the human host and the bacterial microbiota
  - Promotes epithelial cell function, supports nutrient absorption and limits pathogen invasion
- **Crosstalk** between the communities of bacteria and the host influences immune system

Microbiome , its structure and function

- Communities of gut microbiota
  - Viruses,
  - archaea,
  - fungi and
  - certain parasites
- **Juxtaposition** to a highly complex mucus layer that protects the epithelium from bacteria invasion, which allows passage of many small molecules

Main function of Intestinal epithelium

- Provide physical and biochemical barrier to the external environment
- Food components acting directly on immune cells (Vit-A & D)
- Bacterial enzymatic digestion (colon)

Main function of Intestinal epithelium

- Dietary fibers → SCFA
- Regulatory T-cell - Anti inflammatory through the inhibition of
  - the NF-kB signaling and
  - the bacterial lipopolysaccharide-induced inflammatory cascade

Fig 1: Small Intestine mucosal immune system landscape

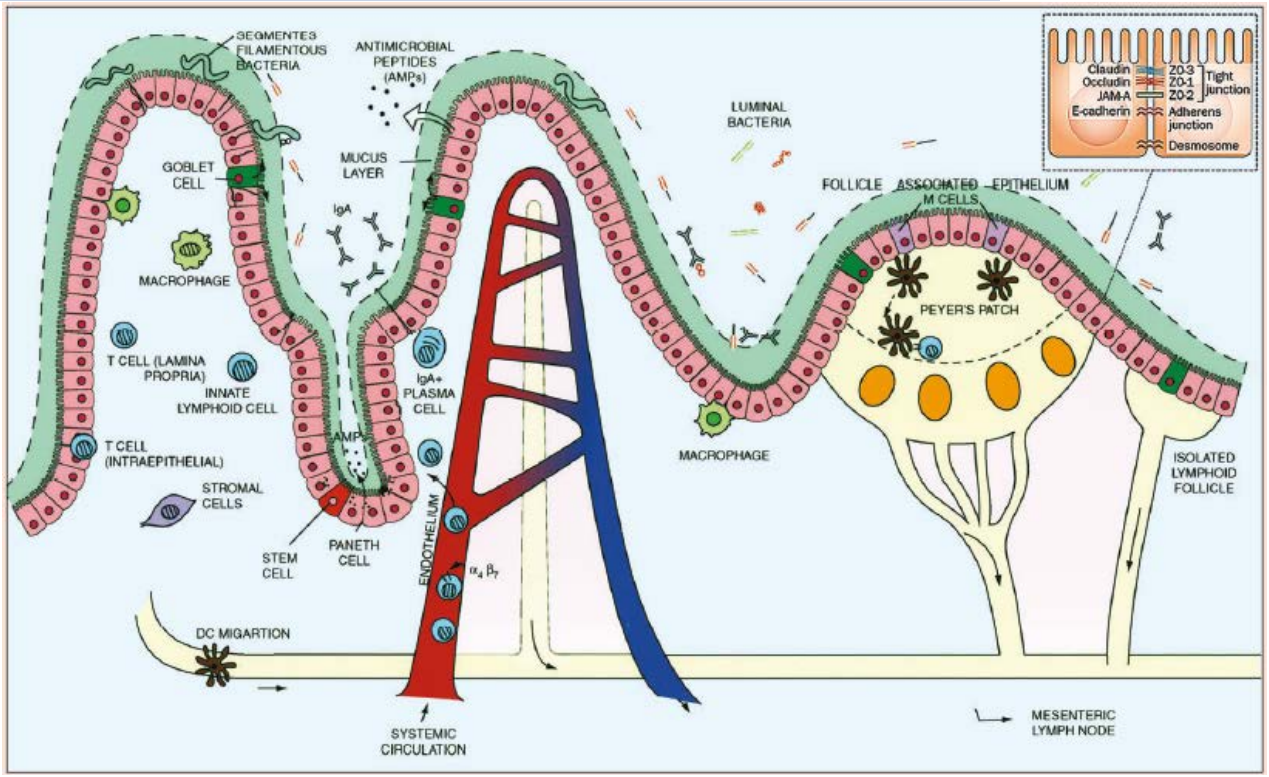
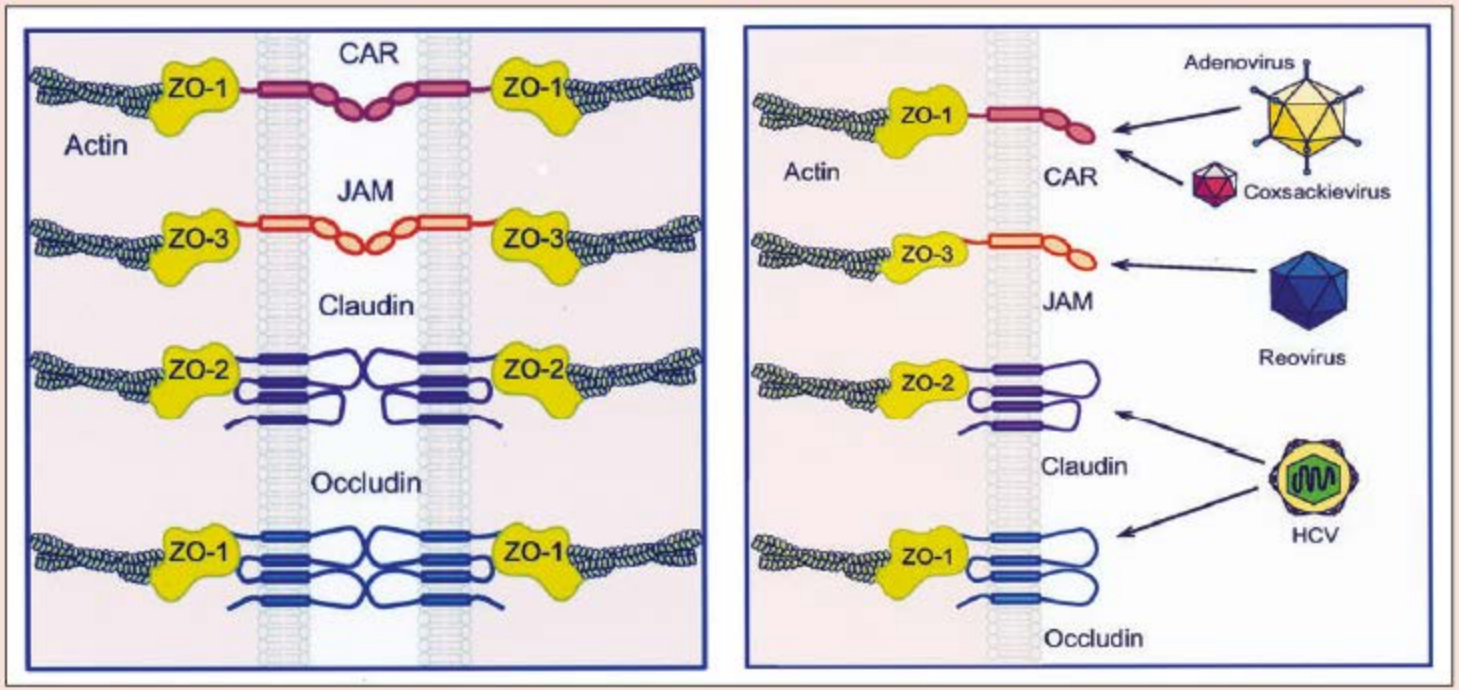
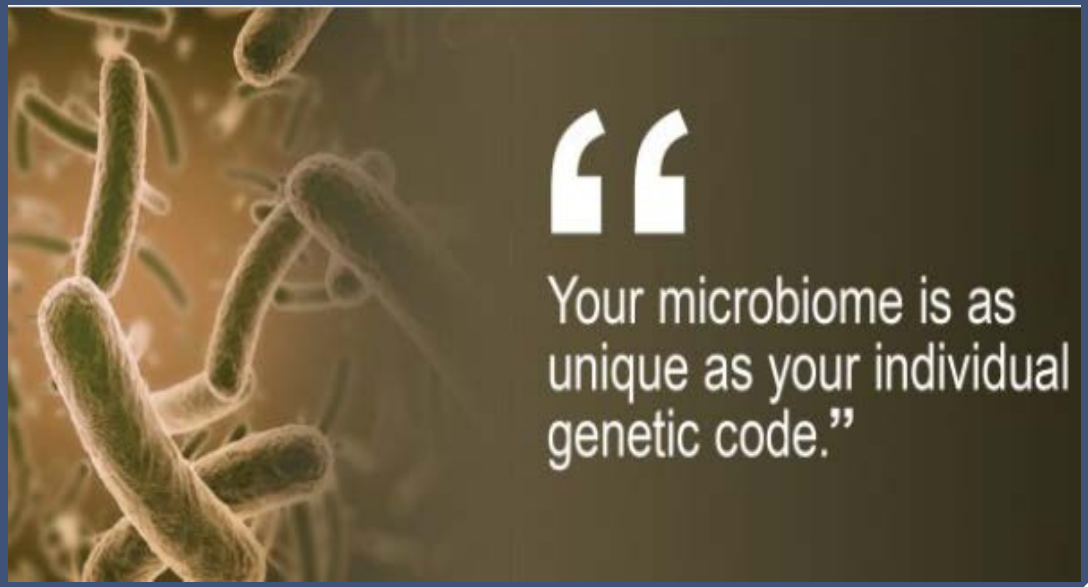


Fig 2: Main component of tight junction of epithelium cells



Type 1 diabetes and gut microbiome

- **T 1 DM** is one of the most common chronic auto-immune diseases in children and adolescents
- The incidence of T1 DM has increased worldwide over the last three decades
- **Genetics:** Human leucocyte antigen (HLA) haplotypes involving Class II DR-DQ region (Insulin and GAD)
- (over 60 genetic markers)


Your microbiome is as unique as your individual genetic code.”

Type 1 diabetes and gut microbiome

- **Gut Microbiome:**
- Intestinal Tract is colonized by a microbial community (Immune mediated diseases)
- Decrease in the diversity of the intestinal microbiota

⬆ Bacteroidetes ⬇ butyrate producing and mucin degrading bacteria

⬇ Tolerogenic T cells

Type 1 diabetes and gut microbiome

- **Immune System Changes:** beta cell damage by CD4+ and CD8+ T cells
- Key to the process of immunological tolerance are so-called regulatory T-cells (Tregs)
- **Viral Link:** Tl DM precipitates in genetically susceptible individuals– Environmental trigger
- Insulitis and apoptosis


Keeping the Creepy Crawlies in your
Gut Microbiome
happy is essential for good
blood sugar control!

Type 2 diabetes and gut microbiome

- An altered gut microbiota can cause dysbiosis that can contribute to metabolic disorders such as type 2 diabetes (T2DM)
- Lipopolysaccharides and short chain fatty acids that are affected by diet, influence metabolic pathways related to T2DM including
  - insulin signaling, appetite regulation, incretin production and inflammation

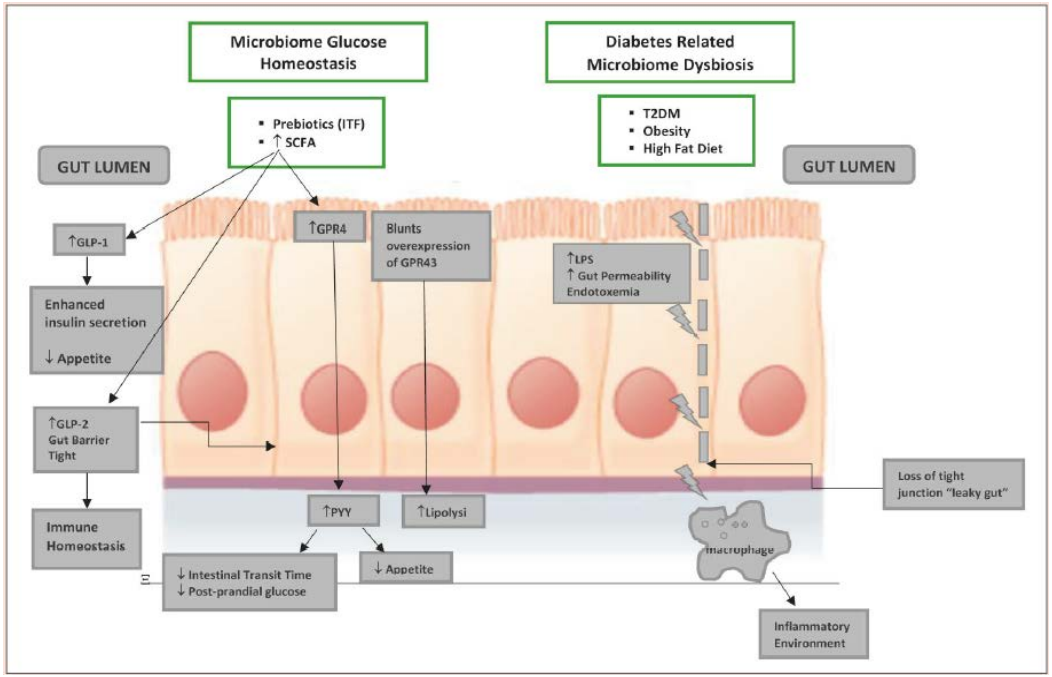
Type 2 diabetes and gut microbiome

- Gut microbiota with low diversity was associated with
  - increased serum leptin, decreased serum adiponectin, insulin resistance, hyperinsulinemia, increased levels of serum triglycerides, decreased high-serum triglycerides, decreased high-cholesterol) and increased highly-sensitive C-reactive protein (hsCRP)

Type 2 diabetes and gut microbiome

- T2DM is associated with a variety of changes in the phyla and certain species within the microbiota
- Increased LPS concentrations and decreased SCFA production can contribute to low grade inflammation, insulin resistance and T2DM

Fig 3: Healthy and Unhealthy Microbiome



Medications and gut microbiome

- Certain bacteria species in our gut are known to aid the production of certain vitamins, such as biotin, B-vitamins, folic acid and vitamin K, and play a major role in metabolic processes and immune function
- Medications affect the gut microbiome
- **Non-steroidal anti-inflammatory drugs** (NSAID)are used to reduce inflammation, lower fevers, reduce blood clotting, and relieve pain.

Medications and gut microbiome

- NSAIDs can change the composition and diversity of gut microbiota towards a pro-inflammatory state, which can influence the effectiveness of the medication

Medications and gut microbiome

- **Proton pump inhibitors** (PPIs) have mainly been used to treat gastrointestinal (GI) disorders, such as bleeding peptic ulcers and acid reflux, to prevent stress ulcers, and to reduce GI toxicity caused by various medications.

Medications and gut microbiome

- Prolonged use of PPIs lead to iron and vitamin B12 deficiencies, hypomagnesemia, osteoporosis-related fractures, community-acquired pneumonia and overgrowth of small intestinal bacteria.

Medications and gut microbiome

- These are caused by dysbiosis within gut flora, due to acid suppression and the induction of hormonal changes, resulting in a greater abundance of bacteria from the mouth and upper GI tract

Medications and gut microbiome

- Animal models have demonstrated that the effect of PPIs on gut flora lead to elevation of serum gastrin levels, which increases proliferation of beta cells and provides a positive effect on glycemic control

Medications and gut microbiome

- **Antibiotics** lead to reduction in bacterial diversity, stimulation of the transfer of genetic information across bacteria, and support the emergence of bacterial resistance.
- Changes within microbiome construction lead to changes in resource availability which enhances the growth of opportunistic pathogens.

Medications and gut microbiome

- Interactions between gut flora can also disrupt glucose homeostasis (decreases insulin sensitivity and glucose tolerance), increase lipid deposition, energy harvesting capacity and weight gain and hence T2DM

Medications and gut microbiome

- **Biguanide** change the makeup of gut microbiota, resulting in several changes, including enhancement of GLP-1 secretion which is beneficial by decreasing insulin resistance.
- Alterations in gut flora induced by metformin include an increase in butyrate producing bacteria.

Table 1: Medications and gut flora

DRUG	ACTION OF MEDICATION	DO GUT FLORA AFFECT THE DRUG?
Metformin	Blood glucose lowering	Yes, enhanced microbiota from Metformin can reduce the side effects associated with the drug and has the potential to contribute indirectly and directly to the glycemic capabilities.
Acetaminophen	Analgesic and antipyretic	Yes, decreases metabolism and increases toxicity risk.
Digoxin	Cardiac Inotropic and Antiarrhythmic agent	Yes, reduces efficacy of drug by altering metabolism and inactivation by microbiota.
Metronidazole	Antibiotic for parasitic and bacterial infections	Yes, inactivation leads to lowered effect and resistance to metronidazole.
Sulindac	Non-steroidal anti-inflammatory drug (NSAID)	Yes, reductive metabolism, accelerated elimination with shortened half-life. Activates the NSAID.

Healthy microbiome, eating habits and lifestyle factors

- The microbiota can improve nutritional status by aiding in digestion, extracting nutrients, and synthesizing vitamins and certain amino acids

Healthy microbiome, eating habits and lifestyle factors

- **Prebiotics** promote the growth of beneficial bacteria that can reduce endotoxemia and gut permeability, and in turn, increase insulin sensitivity and decrease low grade inflammation

Healthy microbiome, eating habits and lifestyle factors

- **Probiotics** help body to produce vitamins, **absorb nutrients** from your food, and even help regulate the **mood**.

Healthy microbiome, eating habits and lifestyle factors

- A study evaluated the microbiota of 153 individuals following a vegan, vegetarian, or omnivore eating pattern. The vegan group consumed more fruits, vegetables, and legumes than the vegetarian and omnivore groups, and had the healthiest microbiota with the highest amounts of SCFA production

Healthy microbiome, eating habits and lifestyle factors

Dietary Advice

- increase intake of fruits and vegetables
- increase fiber intake
- decrease intake of simple sugars/ added sugars
- choose more whole grains and legumes, limit refined carbohydrate sources

Healthy microbiome, eating habits and lifestyle factors

Dietary Advice…

- be mindful of total fat intake and switch to healthier fat sources
- decrease total caloric intake to achieve 5 - 7%weight reduction if overweight
- choose lean protein sources and/or include more vegetable protein options
- limit sodium intake

Healthy microbiome, eating habits and lifestyle factors

Lifestyle Advice

- limit sedentary activity and get at least 150 minutes of aerobic exercise weekly
- engage in some type of resistance exercise two to three times a week
- practice stress-reducing activities and aim for seven to eight hours of sleep nightly
- consider smoking cessation and get regular health check-ups

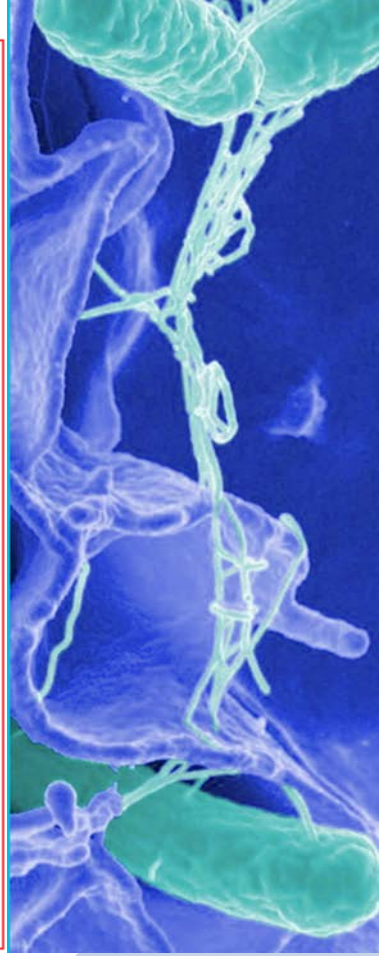
Does it work?

Food for thought

Take Home Message

KEY MESSAGES

- Gut microbiota influences many areas of human health from innate immunity to appetite and energy metabolism
- Targeting the gut microbiome, with probiotics or dietary fibre, benefits human health and could potentially reduce obesity
- Drugs, food ingredients, antibiotics, and pesticides could all have adverse effects on the gut microbiota
- Microbiota should be considered a key aspect in nutrition; the medical community should adapt their education and public health messages
- Fibre consumption is associated with beneficial effects in several contexts



THANKS!

Any questions?

Self Assessment

1. Which of the following complications is associated with prolonged use of proton pump inhibitors (PPI)?

a. Vitamin B-12 toxicity
b. Hypermagnesemia
c. Iron deficiency
d. Peptic ulcers

Self Assessment

2. Which of the following medications is associated with the enhancement of glucagon-like peptide (GLP) 1 secretion?

a. Nonsteroidal anti-inflammatory drugs

b. Thiazolidinediones

c. Proton pump inhibitors

d. Biguanides

Self Assessment

3. Gut microbiota with low diversity is associated with decreased serum levels of:

a. Leptin

b. Adinopectin

c. Triglycerides

d. Insulin

Self Assessment

4. Which of the following biomarkers are increased by prebiotic consumption?

a. Endotoxins

b. C-Reactive proteins

c. Gut permeability

d. Insulin sensitivity

Self Assessment

5. Luminal bacteria are kept from direct contact with the intestinal epithelial cells by:

a. Defensins produced by Goblet cells

b. Mucus produced by the Paneth cells

c. Macrophages found in the tight junctions

d. Tight junctions between the endothelial cells

Self Assessment

6. Which of the following statements is correct about zonulin?

a. It belongs to a family of cysteine proteases

b. It is a homologue of zonula occludins toxin

c. It has an effect to decrease intestinal permeability

d. It is released mostly after viral and bacterial infection

Self Assessment

7. How is gut microbiota associated with the activation of immune response?

a. Microbiota composition may influence the proliferation of B-cells

b. Microbiota abundance may impact the metabolism of dietary fibers

c. Microbiota composition may cause hypo-responsiveness to antigens

d. Microbiota abundance may affect the production of medium-chain fatty acids

Self Assessment

8. Which statement about "diet hypothesis" is correct?

a. The oral tolerance process is particularly vulnerable during puberty

b. Changes in diet are most likely to prime the small intestine to react less aggressively to new antigens

c. It was developed to explain the differential incidence of T1 DM among countries with different food cultures

d. Certain nutrients are involved in a process that results in a shift in the balance between regulatory and effector T-cells

Self Assessment

9. According to the Adventist Health Study-2, which of the following eating patterns conferred the greatest benefit at reducing the risk of developing diabetes?

a. Semi-vegetarian
b. Pesco vegetarian
c. Lacto-ovo-vegetaria
d. Vegan

Self Assessment

10. Which of the following terms is defined as live organisms which when administered in adequate amounts, confer a health benefit to the host?

a. Probiotics
b. Prebiotics
c. Microbiota
d. Microbiome

Self Assessment KEY

1. C
2. D
3. B
4. D
5. D
6. B
7. B
8. D
9. D
10. A

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