RSSDI Indian Diabetes

EDUCATOR JOURNAL

Theme of the Month

Diabetes and Gut Health

To keep Members of Diabetes Care team abreast about
DSME/DSMS - (Diabetes Self management Education/Support) Concepts

2015 2016 2017 2018 2019 2020 2021 2022 2023 2024

Longest Running Monthly Journal

In collaboration with USV

RSSDI

(RESEARCH SOCIETY FOR THE STUDY OF DIABETES IN INDIA)

Launches the Largest Obesity Awareness Campaign

WEIGHT MATTERS

Scan the QR Code to Participate

In Association With

USV

RSSDI
Indian
Diabetes
EDUCATOR JOURNAL

1 st time in India
To keep the members of diabetes care team abreast with DSME and DSMS concepts

EDITORIAL BOARD

Scan the QR code to access full library of IDEJ - **https://usvmed.com/**

*DSME: Diabetes Self-Management Education, DSMS: Diabetes Self-Management Support

NATIONAL ADVISORY BOARD

RSSDI Indian Diabetes
EDUCATOR JOURNAL

1 st time in India
To keep the members of diabetes care team abreast with DSME and DSMS concepts

FOREWORD

Research Society for the Study of Diabetes in India (RSSDI) founded by Prof MMS Ahuja in the year 1972 is the biggest scientific association of healthcare professionals involved in promoting diabetes education and research in India. RSSDI is happy to collaborate with USV to support their endeavour to make India the 'Diabetes care capital of the world'. Through this collaboration, RSSDI would like to strengthen the cadre of diabetes educators by empowering them with recent updates in diabetes management helping bridge the gap between the physician and the patient. Today, the rule of 50% is prevailing in terms of awareness, detection, treatment and control in T2DM. Our aspiration is to achieve 90-90-90-90 i.e.90% of people with diabetes should be made aware, 90% should be detected, 90% of those detected should be treated, and 90% of those treated should reach their goals.

Indian Diabetes Educator Journal (IDEJ) is the first of its kind in India, and the longest running monthly diabetes educator journal since April 2015 & continues its endeavour to spread awareness, knowledge and enable healthcare teams to manage individuals with diabetes and empower them for self-care. RSSDI IDEJ will continue to keep the members of diabetes care team abreast with concepts of Diabetes Self-Management Education/Support (DSME/S) with a reach of 44000 doctors and diabetes educators digitally.

World Digestive Health Day is celebrated every year on 29th May. This month's IDEJ aims to explore the connection between diabetes and related gut disorders such as gastroparesis. As a metabolic disorder, diabetes can impact the functionality of the nervous system and may contribute to the occurrence or risk of gastroparesis. Gut health has also been implicated in the risk of developing diabetes and its complications. It is imperative for diabetes educators to comprehend the interrelation between diabetes and associated gut-related disorders, ensuring a comprehensive approach for individuals dealing with diabetes. We anticipate that this edition will equip diabetes educators with valuable clinical insights within the realm of diabetes and gut health.

We sincerely thank our contributors for making this issue delightful reading for our readers. We dedicate this journal to all the healthcare professionals who are working relentlessly towards making "India–The Diabetes Care Capital of the World."

Sincere Regards,

Dr. Sanjay Agarwal
RSSDI Secretary

*DSME: Diabetes Self-Management Education, DSMS: Diabetes Self-Management Support

Expert Contributors
of the month

Dr. Rajesh Mistry

MD, MSU

Consulting Physician and Clinical Cardiologist, Heart Care, Navsari

Article: Inter-relationship between Gut microbiota and Diabetes

Dr. Indumathi Kuberan

MBBS, Fellowship in Diabetes (CMC Vellore)

Consultant Diabetologist, Indu's Diabetes Clinics, Mumbai

Article: Diabetes-associated Gut Complication: Gastroparesis

Dr. Ronak Shah

MD (Medicine)

Consultant Physician, Aagam Hospital, Anand

Article: Management of Gastroparesis

Dr. Ghanshyam V. Patel

MBBS, MD (Medicine)

Consultant Physician, Suchi Hospital, Surat

Article: Therapeutic Value of Harnessing Gut Microbiota

Dr. Arvind Gupta

MD, FRCP (Glasgow), FRCP (Edin), FACP (USA), FICP, FACE (USA)

Senior Consultant, Department of Internal Medicine and Diabetes, RHL-Rajasthan Hospital, Jaipur

Article: Interview with Dr. Arvind Gupta

Dr. Manish Agarwal

MD, PhD, PGDDM, FACP (USA), Diploma in Endocrinology

Consultant Diabetologist and Metabolic Physician, Medilink Hospital, Ahmedabad

Article: Oral Antidiabetic Medications and Gut Microbiome

Expert Contributors
of the month

Dr. Devi Gayathri Palanivel

MBBS, DNB (Internal Medicine), PG Diploma in Diabetes

Consultant Physician and Diabetologist, Royal Care Super Speciality Hospital, Coimbatore

Article: Gut Microbiota and Complications of Diabetes

Dr. Vedavati Purandare

MBBS, MD (Medicine), PhD

Clinical Head, Consultant Physician and Diabetologist, Chellaram Diabetes Institute, Pune

Article: Role of Gut Microbiota in Type 1 Diabetes Pathophysiology

Dr. Saurabh Agarwal

MBBS, MD (Manipal), FIDM (UK), FAGE, CCID (UK), CCEBDM

Consultant Physician and Diabetologist, Swasthyam Medical Clinic, Lucknow

Article: Diabetes and Gut Friendly Foods

Dr. Ega Lakshman Kumar

MD (Gen Medicine), DM (Endocrinology)

Consultant Endocrinologist, Padmakshi Polyclinic, Warangal

Article: Frequently Asked Questions on Diabetes and Gut Health

To get featured in the Indian Diabetes Educator Journal you can connect with us on the below mail ID for further communication: info@nurturehealthsolutions.com

RSSDI Indian Diabetes
EDUCATOR JOURNAL

Issue No. 110, May 2024

Table of Content

Cover Story: Inter-relationship between Gut Microbiota and Diabetes

Dr. Rajesh Mistry

MD, MSU

Consulting Physician and Clinical Cardiologist, Heart Care, Navsari

Diabetes mellitus, a metabolic disorder affecting glucose regulation, is a significant global health concern, affecting around 74.2 million people in India. Predictions by the International Diabetes Federation estimate a rise to 124.9 million cases by 2045 (IDF Diabetes Atlas, 10th Edition 2021) with type 2 diabetes being the most prevalent form, linked to factors such as obesity, sedentary lifestyle, poor diet, and genetics.

Gut microbiota and diabetes

The gut microbiome, vital for digestion and immune function, produces short-chain fatty acids and gases through fermentation. Dysbiosis caused by factors such as lifestyle, antibiotic use, and dietary changes, is linked to metabolic diseases such as obesity and diabetes mellitus. Dysbiosis in diabetes includes an increase in gram-negative species and a reduction in butyrate-producing species, leading to translocation of bacterial lipopolysaccharide (LPS) into the bloodstream. This affects gut wall integrity, causing endotoxemia and chronic inflammation (figure 1). Reduced butyrate levels also contribute to insulin resistance by impacting glucagon-like peptide-1 (GLP-1) pathway activation, fatty acid oxidation, and thermogenic energy expenditure. Insulin resistance and chronic inflammation exacerbate dysbiosis, worsening diabetes progression, and affecting intestinal epithelium, nerves, and blood vessels.

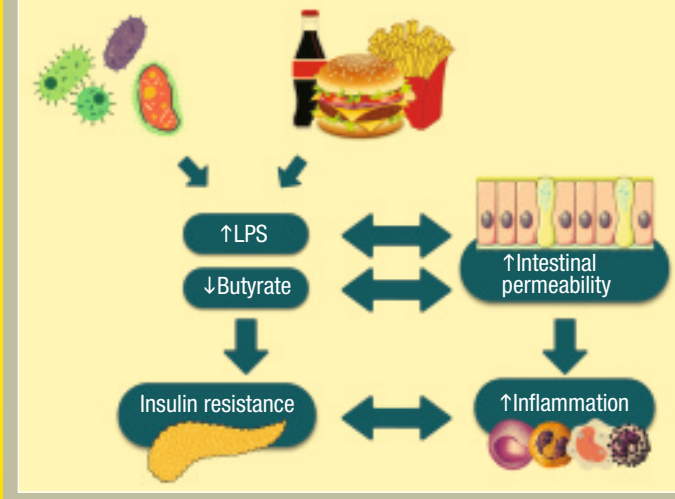


Figure 1. Dysbiosis in diabetes pathogenesis
Abbreviations: LPS: Lipopolysaccharide

Effect of diabetes on gut microbiota

Gut microbiome of individuals with diabetes are found to have a prevalence of pathogenic and opportunistic gram-negative species at the expense of commensal ones. An increase in pathogenic bacteria, such as Enterobacteriaceae, various Clostridiales, *Escherichia coli, Bacteroides caccae*, and *Lactobacilli*, as well as *Prevotella copri* and Bacteroides vulgates, have been reported in the microbiota of individuals with diabetes. The therapeutic efficacy and potential side effects with the administration of antidiabetic drugs are also influenced by resident microbiota (shown in figure 2) and the presence of certain genera/species could predict whether individuals will experience side effects as well as their response to probiotic supplementation.

Therefore, gut microbiota emerges as a new prognostic biomarker in diabetes, underscoring the need for additional research to evaluate the therapeutic potential of gut microbiota manipulation with prebiotics and probiotics supplementation. Dietary adjustments aimed at restoring gut microbiota in people with diabetes could serve as a complementary strategy to enhance response to drug therapy and promote better adherence by mitigating adverse effects.

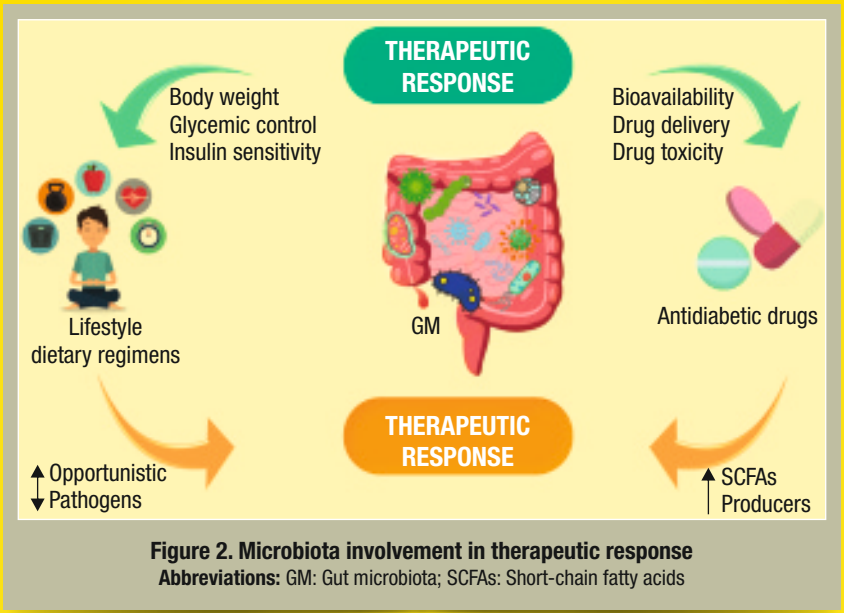


Figure 2. Microbiota involvement in therapeutic response
Abbreviations: GM: Gut microbiota; SCFAs: Short-chain fatty acids

Resources:

1. Crudele L, Gadaleta RM, Cariello M, Moschetta A. Gut microbiota in the pathogenesis and therapeutic approaches of diabetes. *eBioMedicine.* 2023;97:104821. doi:10.1016/j.ebiom.2023.104821
2. Li WZ, Stirling K, Yang JJ, Zhang L. Gut microbiota and diabetes: From correlation to causality and mechanism. *World J Diabetes.* 2020;11(7):293-308. doi:10.4239/wjd.v11.i7.293
3. Craciun CI, Neag MA, Catinean A, *et al.* The Relationships between Gut Microbiota and Diabetes Mellitus, and Treatments for Diabetes Mellitus. *Biomedicines.* 2022;10(2):308. Published 2022 Jan 28. doi:10.3390/biomedicines1002030

Diabetes-associated Gut Complication: Gastroparesis

Dr. Indumathi Kuberan

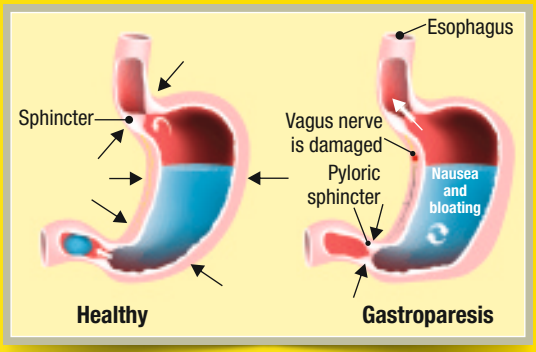
MBBS, Fellowship in Diabetes (CMC Vellore)

Consultant Diabetologist, Indu's Diabetes Clinics, Mumbai

Diabetes is the most widely known cause of gastroparesis with high blood glucose levels over a long period being the main causative factor. The delay in gastric emptying without any indication of mechanical obstruction resulting from impaired coordination and defect in the function of muscle cells of the gastrointestinal tract, autonomic nervous system, and neurons is known as gastroparesis.

Etiology of gastroparesis in diabetes

Dysfunction in gastric emptying results from complex interactions involving autonomic and enteric nervous systems, smooth muscle cells, and specialized pacemaker cells. As a result, most individuals with diabetes face issues at different points of gastric emptying. This dysfunction encompasses issues in postprandial proximal gastric accommodation, contraction, and antral motor function.

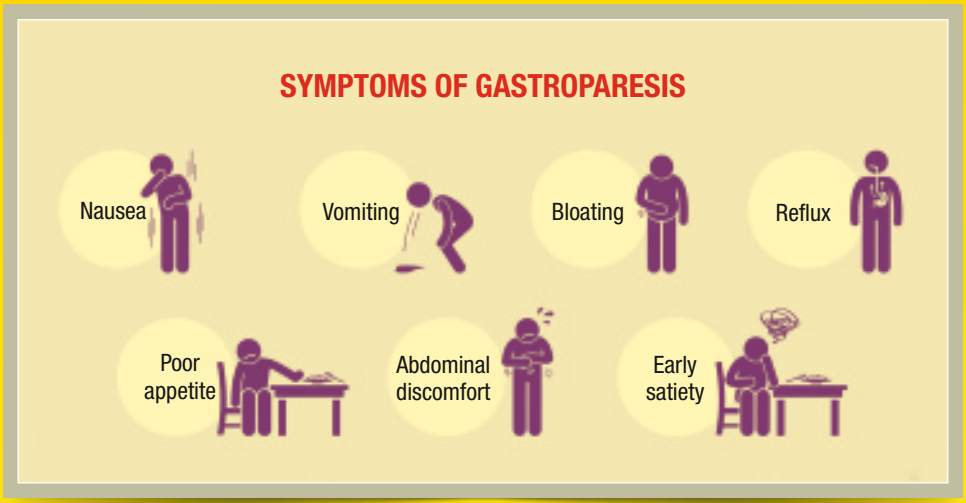


Prevalence

Although there is a stronger link between type 1 diabetes and gastroparesis, the prevalence of type 2 diabetes is significantly higher, hence gastroparesis linked with type 2 diabetes is more common. It has also been observed that gastroparesis often occurs in individuals with a diabetes diagnosis of at least ten years, making it more common in elderly people with type 2 diabetes.

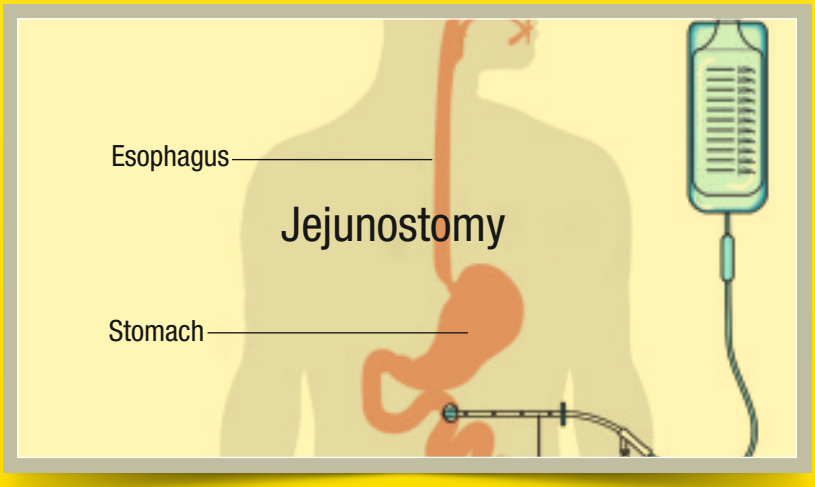
Symptoms

Nausea is the predominant symptom of gastroparesis. Other prevalent symptoms include vomiting, feeling full soon after eating, bloating, and postmeal discomfort. Weight loss or gain may occur, along with significant glycemic fluctuations. The timing of symptoms concerning meals is crucial. While physical examination is typically nonspecific, individuals with diabetic gastroparesis may exhibit neuropathy, abdominal distension, and halitosis (bad breath). Triggers for exacerbation include uncontrolled blood glucose levels, medication noncompliance or intolerance, and infection.



Complications and risks

Malnutrition is a significant complication in diabetic gastroparesis, often requiring management through jejunostomy, parenteral nutrition, or surgery. Diabetic gastroparesis may cause wide glycemic fluctuations, leading to complications like hypoglycemia, diabetic ketoacidosis, or hyperosmolar hyperglycemic state. Nausea and vomiting increase the risk of aspiration pneumonia.



Diabetic gastroparesis treatment seeks to reduce symptoms while also replenishing nutritional status. Effectively managing diabetic gastroparesis poses significant challenges. The most effective approach involves collaboration among the multidisciplinary team, including an endocrinologist, nurse, gastroenterologist, dietitian, and diabetes educator. Patient education and consultation with a diabetes educator can greatly improve the clinical outcomes of this disease.

Key points

- Diabetes is a well-known cause of gastroparesis affecting the digestion process. Impaired digestion occurs due to dysfunction in gastric emptying and involves complex interactions among the autonomic and enteric nervous systems, smooth muscle cells, and specialized pacemaker cells.
- Symptoms of gastroparesis include nausea, vomiting, bloating, and post-meal discomfort. Triggers for exacerbation include uncontrolled blood glucose, medication issues, and infections.
- Dietary modifications, pharmacotherapy, and physical activity are key components in the management of symptomatic gastroparesis aimed at maintaining blood glucose levels.

Resources:

1. Diabetes and Digestion. Centers for Disease Control and Prevention. Updated July 28, 2022. Accessed February 5, 2024. Available at: https://www.cdc.gov/diabetes/library/features/diabetes-digestion.html
2. Aswath GS, Foris LA, Ashwath AK, et al. Diabetic Gastroparesis. [Updated 2023 Mar 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430794/

Management of Gastroparesis

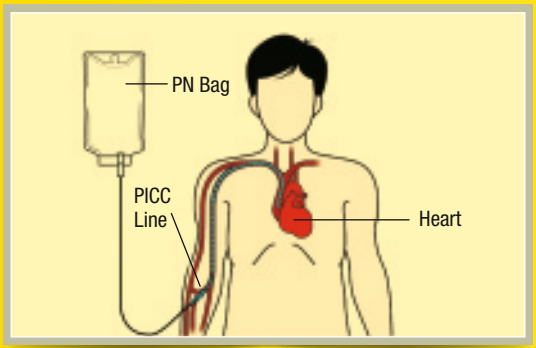
Dr. Ronak Shah

MD (Medicine)
Consultant Physician, Aagam Hospital, Anand

The management of gastroparesis requires a multifaceted approach that includes lifestyle modifications, pharmacotherapy, and in refractory cases, interventional and surgical treatments.

Lifestyle modifications

The initial step in treating symptomatic gastroparesis often involves lifestyle modifications aimed at optimizing gastric function and alleviating symptoms. For individuals with diabetes, achieving optimal glycemic control is paramount to minimize the effects of hyperglycemia on gastric emptying. Additionally, dietary adjustments play a crucial role in symptom management, with recommendations emphasizing to consume small frequent meals which are low in fat and fiber to reduce symptoms such as nausea, vomiting, and abdominal discomfort. They are advised to avoid spicy, acidic, and high fat foods, as well as carbonated beverage consumption, quit smoking, and restrict alcohol intake, as these habits can exacerbate gastroparesis symptoms.



In more severe cases, nutrition supplementation with homogenized or liquid meals may be necessary, and enteral or parenteral nutrition may be indicated for individuals who are unable to ingest solid foods, especially if weight loss indicating undernutrition is predominant. Glycemia control is essential but challenging due to unreliable food absorption and delayed gastric emptying. Dose adjustments for mealtime insulin may be necessary to match the delayed postprandial glucose rise. Including regular physical activity (minimum of 150 minutes of physical activity per week) as part of a holistic approach is also important. However, as the disease progresses, nutritional approaches alone may not suffice, necessitating pharmacological or surgical interventions.

Pharmacological interventions

Pharmacological therapy forms the cornerstone of treatment for gastroparesis, with several medications aimed at improving gastric motility and alleviating symptoms. Antiemetics, such as serotonin (5-HT3) receptor antagonists like ondansetron and dopamine receptor antagonists like prochlorperazine and promethazine, are commonly used to relieve nausea and vomiting. However, these medications may have side effects such as sedation and extrapyramidal effects and are generally administered on an as needed basis.

Prokinetic agents are another class of medications frequently utilized in the management of gastroparesis. Metoclopramide, a dopamine receptor antagonist and 5-HT4 receptor activator, enhances gastric emptying by increasing muscle contractions. Similarly, erythromycin, which binds to motilin receptors responsible for initiating gastric contractions, can also improve gastric motility. Keeping the doctor informed about all medications and supplements is also important as certain medications may cause digestive difficulties.

Interventional and surgical treatments

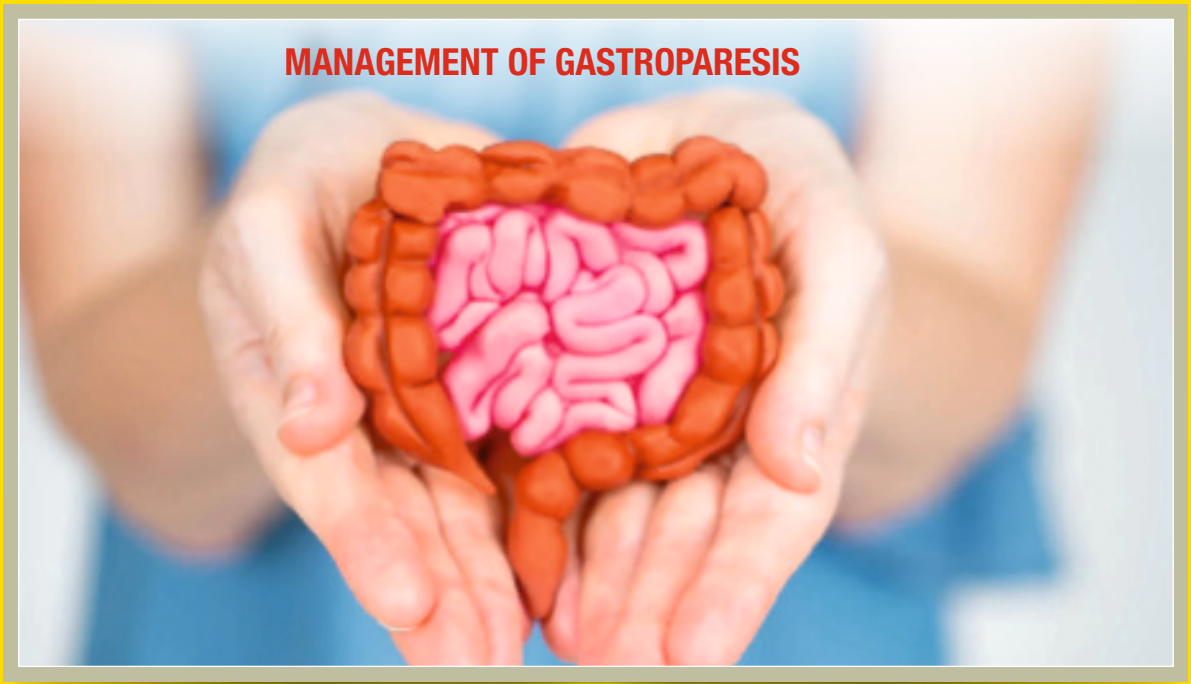
When pharmacological therapy fails, interventional and surgical options may be considered for severe symptoms of gastroparesis. Gastric electrical stimulation and endoscopic techniques like botulinum toxin injections or balloon dilation can improve gastric motility. In refractory cases, gastrostomy or jejunostomy tubes may be placed for decompression or feeding. Surgical options like partial gastrectomy are considered a last resort and should be decided upon with the guidance of a motility expert due to limited evidence supporting their efficacy.

Key points

- A multidisciplinary approach involving dietary, pharmacological, and surgical interventions assists in symptom management and enhances quality of life.
- Lifestyle modifications play a crucial role in managing gastroparesis, including dietary modifications such as small frequent meals, avoidance of exacerbating factors like spicy and high-fat food, alcohol intake, physical activity, and consideration of nutrition supplementation in undernourished individuals.
- Pharmacological interventions form the cornerstone of treatment with antiemetics and prokinetic agents commonly used to alleviate symptoms and improve gastric motility.
- Interventional and surgical treatments may be necessary in refractory cases, including gastric electrical stimulation, botulinum toxin injections, or surgical placement of feeding tubes.

Resources:

1. Usai-Satta P, Bellini M, Morelli O, Geri F, Lai M, Bassotti G. Gastroparesis: New insights into an old disease. *World J Gastroenterol.* 2020;26(19):2333-48. doi:10.3748/wjg.v26.i19.2333
2. Aswath GS. Diabetic gastroparesis. *StatPearls [Internet].* March 2023.
3. Young CF, Moussa M, Shubrook JH. Diabetic gastroparesis: A Review. *American Diabetes Association.* August 2020.



Therapeutic Value of Harnessing Gut Microbiota

Dr. Ghanshyam V. Patel

MBBS, MD (Medicine)

Consultant Physician, Suchi Hospital, Surat

Diabetes management has majorly focused on combining drugs with a healthier diet and a physically active lifestyle. Evidence suggests a significant role of gut microbiota in the etiology of diabetes as well as altered microbiota existing in individuals with diabetes. Improving gut microbiota can serve as a valuable adjuvant measure in reducing diabetes risk as well as improving overall health in individuals with diabetes. One of the common ways to improve gut microbial balance is the use of probiotics, prebiotics, or a combination of both called as synbiotics.

Probiotics

Probiotics are live microorganisms that can confer health benefits when consumed in adequate amounts. Yogurt, kimchi, kefir, kombucha, fermented pickle, kanji (black carrot), fermented rice (Panta bhaat) are some of the sources. Probiotics exert a multifaceted influence on the composition of the gut microbiota. This includes various actions such as inhibiting alpha-glucosidase activity, producing lactic acid, enhancing the integrity of the intestinal barrier, modulating the immune system, generating short-chain fatty acids (SCFAs), and regulating bile acid metabolism, among other mechanisms. Treatment with probiotics, especially some *Lactobacillus* and *Bifidobacterium* strains, have shown to improve fasting glucose levels, HbA1c levels, and also improve lipid profile.

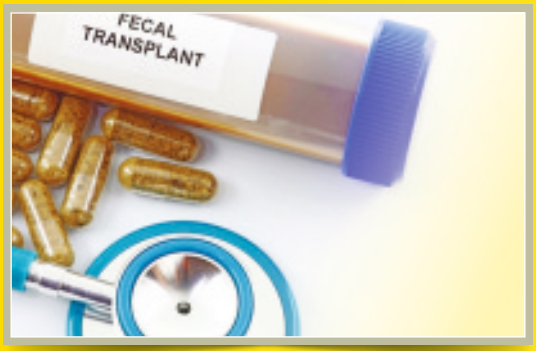
Administering a combination of probiotics has demonstrated positive effects on glucose control, however, these benefits have primarily been observed in murine models. In human studies, the outcomes have not been as significant, particularly when compared to gold-standard diabetes treatments. This suggests that while probiotics may serve as an adjunctive therapy, they are not curative on their own.

Prebiotics

Prebiotics are non-digestible fibers that promote the growth and activity of beneficial bacteria in the gut. Sources include whole grains, legumes, garlic, vegetables like onion, leeks, raw banana, jackfruit seeds and also raw banana, apple, pear, etc. Prebiotic fiber has shown positive effects on glucose homeostasis, inflammation and leptin sensitivity, GLP-1 production, intestinal epithelial integrity.

The ability of prebiotics to potentiate drug therapy has been widely demonstrated, and therefore, combining drug therapy with prebiotics and probiotics could significantly improve hyperglycemia and also obesity.

Diabetes and fecal microbiota transplantation (FMT)



Another strategy to harness the microbiota as an adjuvant is FMT, also known as stool transplantation. The transfer of stools from a healthy donor to another subject's gastrointestinal tract, seeking to change the recipient's gut microbiota gaining health benefits. Emerging evidence suggests the beneficial role of FMT in diabetes, more long-term clinical trials are needed to arrive at a recommendation. Successful microbial modulation will depend on the strain, its composition and diversity, and also on the individual's pre-existing microbial diversity. But, there are some risks associated with FMT that must be taken into account such as the transfer of infectious disease.

While research is inconclusive on the therapeutic recommendation of probiotics and prebiotics, their inclusion in the diet can be advised as a complementary approach for holistic diabetes management.

Resources:

1. Crudele L, Gadaleta RM, Cariello M, Moschetta A. Gut microbiota in the pathogenesis and therapeutic approaches of diabetes. *EBioMedicine.* 2023;97:104821. doi:10.1016/j.ebiom.2023.104821

Interview with Dr. Arvind Gupta

Dr. Arvind Gupta

MD, FRCP (Glasgow), FRCP (Edin), FACP (USA), FICP, FACE (USA)

Senior Consultant, Department of Internal Medicine and Diabetes, RHL-Rajasthan Hospital, Jaipur

Dr. Arvind Gupta is a senior consultant diabetologist at Rajasthan Hospital with a vast experience of over 34 years in this field. He is also the director and senior consultant at Jaipur Diabetic Centre. His speciality of diabetes, obesity, and metabolic disorder underscores his commitment to addressing critical health concerns. He has published nearly 75 papers in national and international journals related to diabetes and is actively involved in many research studies in the field of diabetes. Dr. Gupta's involvement in both government and private organizations, along with his contributions to numerous research studies, showcases his dedication to advancing medical knowledge and improving patient care. Dr. Arvind Gupta's unwavering dedication to patient care has earned him the trust and admiration of countless individuals whose lives he has positively impacted.

Diabetes and Gut Health

1. How are diabetes and gut health interrelated?

Diabetes can affect many parts of the body, especially the gut. Therefore, people with type 1 or type 2 diabetes experience poor gastrointestinal health. Diabetes-related damage to the gut increases the risk of colon cancer, poor digestion, and intestinal malfunction. It even triggers the gut to become a breeding ground for unhealthy bacteria.

It leads to gas, bloating, stomach pain, diarrhea, and constipation. In addition, due to poor glycemic control, a person with diabetes is twice as likely to experience an abnormal gut function. However uncontrolled diabetes can damage nerves in the intestine which can deteriorate the gut by altering the composition of its bacterial colonies. Also, it can cause undesirable chemical changes in the vagus nerve, which connects the gastrointestinal tract and brainstem. This change causes delayed gastric emptying, meaning that the food remains in the stomach for too long. This leads to nutrient malabsorption and deficiencies. It can cause symptoms like heartburn, reduced appetite, vomiting, and nausea.

The human gut is a complex ecosystem consisting of microbiomes, host cells and nutrients. There are about 100 trillion bacteria in the intestinal tract and they form the gut microbiota. Gut microbes are influenced by diet, genetics, and medication, and common types of interventions in humans include fecal microbiota transplantation, metformin, and probiotics.

The gut microbiome plays a significant role in the metabolism of carbohydrates and fats and can influence the body's ability to regulate blood glucose levels. Studies have found that individuals with type 2 diabetes have a less diverse and less balanced gut microbiome compared to healthy individuals. Studies have suggested that an imbalance in the gut microbiome, known as dysbiosis, can lead to chronic low-grade inflammation, which is a known risk factor for type 2 diabetes.

2. Do you commonly see digestive issues such as constipation, acidity, bloating in individuals with diabetes? What reasons could be attributed to these issues?

We commonly see individuals with diabetes suffering from symptoms that include nausea, vomiting, reduced appetite, feeling full after eating small amounts of food, abdominal pain, and heartburn. While these symptoms are already often debilitating, gastroparesis patients' inability to eat enough can cause many complications. Nutrient deficiencies are common, and these can lead to fatigue, weight loss, and anemia. In some cases, excessive vomiting can cause severe dehydration. Other symptoms include heartburn, nausea, vomiting, and poor appetite.

3. How commonly do you see gastroparesis in individuals with diabetes?

We see around 5% of individuals with symptoms of gastroparesis in type 1 diabetes and around 10-15% in type 2 diabetes. It is very common in individuals with long-duration of diabetes and especially individuals with uncontrolled diabetes. Diabetes is the leading cause of gastroparesis, a condition in which food remains in the stomach for too long (delayed gastric emptying). Gastroparesis is dangerous in diabetes because delayed gastric emptying can lead to periods of very high or very low blood glucose levels. It also affects how the body absorbs nutrients, which can lead to malnutrition if left untreated. Another symptom of gastroparesis is frequent vomiting. This is dangerous because it can cause dehydration or extreme thirst.

4. What suggestions would you give for maintaining gut health?

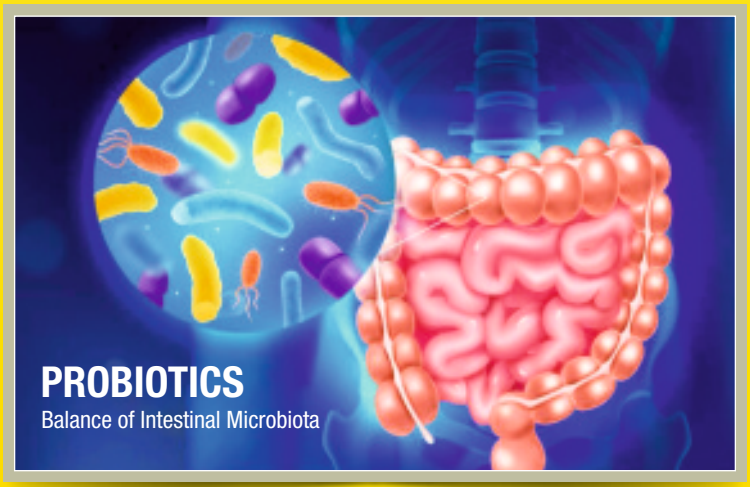
There is no cure for gastroparesis, but gut health can be improved by the following

- **Glycemic control:** Glycemic control is extremely important for the gut health and individuals with diabetes are advised to keep their HbA1c under 7%.
- **Diet:** A diet that is high in fiber, low in sugar, and rich in fermented foods can help to promote a healthy gut microbiome. Consuming a variety of fruits, vegetables, whole grains, and fermented foods such as yogurt, kefir, and sauerkraut can help to support the growth of beneficial bacteria in the gut.

- **Avoid processed foods:** Processed foods are often high in sugar and low in fiber, which can contribute to an imbalance in the gut microbiome. Limiting the intake of processed foods can help to improve gut health.
- **Limit the use of antibiotics:** Antibiotics can disrupt the delicate balance of bacteria in the gut, leading to an overgrowth of harmful pathogens. Hence, antibiotics should strictly be taken under the physician's guidance.
- **Reduce stress:** Stress has been linked to changes in the gut microbiome, so finding ways to manage stress such as yoga, meditation, or therapy can help to improve gut health.
- **Exercise regularly:** Regular exercise has been shown to have a positive impact on the gut microbiome, so incorporating physical activity (minimum 150 minutes a week) into daily routine can help to support gut health.
- **Get enough sleep:** Sleep is the cure for multiple problems. In addition to improving mental well-being, mood, and cognition, getting a sufficient amount of good-quality sleep sustains gut health. Irregular sleep habits, especially among diabetes people, triggers unwanted inflammation. That's because disturbed sleep pattern negatively impacts the gut.
- **Do not eat a heavy dinner:** Even when you're asleep, the gut continues to work. However, consuming large portions during dinner will exert additional pressure on the digestive system. Thus, the gut is deprived of adequate time to rest. As a result, people wake up in the middle of the night with indigestion, acidity, heartburn, or stomach pain. Moreover, a heavy dinner is a big no for those with diabetes as it spikes blood glucose levels.
- **Follow a vegetarian diet:** Studies show that a vegetarian diet for can lower the gut inflammation due to remarkable improvement in gut microbes.
- **Gut-friendly foods for individuals with diabetes:** Kombucha, Kimchi, Oats, Barley, Curd, Onion, Blueberries, and Garlic

5. Should people with diabetes use probiotic supplements?

Probiotics appear to have a wide range of benefits on the host, including improved regulation of insulin sensitivity, which may also be related to host metabolism mediated by the gut microbiome balance, by improving host metabolism composition, by reducing pro-inflammatory cytokines, and by reducing intestinal permeability. In addition, probiotics have the potential to directly improve host metabolism and increase short-chain fatty acid (SCFA) production. Supplementing probiotics can also improve intestinal balance through the production of antibacterial compounds and competition with pathogens. Probiotics may also regulate the host's immune response and activate specific gene activation and impact extra-intestine processes and disorders.



Take home message

Gut health is exceptionally essential for people with diabetes. It is adversely affected by abnormal glucose and insulin fluctuations. Consuming a healthy dose of probiotics, prebiotics, high fiber, and antiinflammatory foods is excellent to boost the gut health.

Staying hydrated throughout the day is also very important to maintain gut health. Drinking adequate water is important along with fiber intake to avail its benefits and for the gut system to run smoothly. In addition, adequate fluid intake is also essential for people with diabetes.

An imbalance in the gut microbiome might weaken the immune system, rendering one susceptible to infections and inflammations. Moreover, an unhealthy gut can also trigger several brain disorders. Hence, maintaining a healthy gut is essential for everyone.

Suggested readings:

1. Iatcu CO, Steen A, Covasa M. Gut Microbiota and Complications of Type-2 Diabetes. *Nutrients.* 2021;14(1):166. doi:10.3390/nu14010166
2. Wei-Zheng Li, Kyle Stirling, Jun-Jie Yang, and Lei Zhang, Gut microbiota and diabetes: From correlation to causality and mechanism. *World J Diabetes.* 2020 Jul 15; 11(7): 293-308. doi: 10.4239/wjd. v11.i7.293
3. Crudele L, Gadaleta RM, Cariello M, Moschetta A. Gut microbiota in the pathogenesis and therapeutic approaches of diabetes. *EBioMedicine.* 2023; 97:104821. doi: 10.1016/j.ebiom.2023.104821
4. Zhou Z, Sun B, Yu D and Zhu C. Gut Microbiota: An Important Player in Type 2 Diabetes Mellitus. *Front. Cell. Infect. Microbiol.* 2022. 12:834485. doi: 10.3389/fcimb.2022.834485

Tailored Nutrition Counseling and Diabetes Education
A Doctor's Experience on the MyCare Patient Support Program

Dr. Sunita Sayammagaru

MBBS, MRGCP (UK), D. Endo (UK), D. Diab (UK), DFRSH (UK), DRCOG (UK)

Consultant Endocrinologist, New Leaf Clinic, Hyderabad

A 68-year-old man with type 2 diabetes was managed by Dr. Sunita Sayammagaru

Here's what Dr. Sunita Sayammagaru has to say:

A patient with high blood glucose levels (HbA1c: 9.4%) sought consultation. Despite maintaining regular meal timings, he remained insulin-dependent due to food cravings. He inquired about managing glucose levels solely through medication.

I sought the guidance of MyCare Diabetes Educator (MDE), Madhurima Das, who played a crucial role in addressing his concerns. She took a detailed dietary recall and advised to maintain a food diary and monitor blood glucose levels at least four times a day. We changed his insulin and medicines, put him on a continuous glucose monitoring system (CGMS), which revealed nighttime glucose spikes to 400s, followed by afternoon declines. Before dinner, he often experienced hypoglycemia and would correct it with sugar/sweets.

She suggested a customized meal plan, educated on carbohydrate quality, stressed the importance of salads, and encouraged walking, meditation, and yoga. She also educated him about insulin technique and dose management. However, he insisted on keeping his current diet of coffee with sugar, parathas, and papaya with meals.

She suggested that one day he could follow his preferred diet, and the next day adhere strictly to the advised diet. The goal was to observe the difference. After counseling him several times, he began to follow the advised diet. He could notice the difference in his glucose levels with the advised diet.

Gradually, his blood glucose levels significantly improved. Fasting blood glucose levels reduced to <115 mg/dL, post lunch is 170-200mg/dL, and HbA1c reduced to 7.5%. After the program ended, he is still following the advised dietary regimen and has maintained his HbA1c at 7.1%.

Ms. Madhurima Das

NDEP and T1DE Certified Diabetes Educator

Here's what MDE Madhurima Das has to say:

I alternated between the patient's preferred diet and a structured meal plan, helping him to observe glucose level variances. With consistent motivation, he gradually adhered to the advised regimen, gaining clarity on food choices and cheat meal allowances.

MyCARE

With me, every step of the way

20 weeks personalised and hand-holding support for people with diabetes initiated with Insulin.
Aims to empower PWD* with information and knowledge they need to
ensure a better quality of life while managing their diabetes.

MyCARE Service available at Ahmedabad, Bangalore, Bhopal, Bhuvaneshwar, Burdwan, Chandigarh, Chennai, Cochin, Coimbatore, Delhi, Guwahati, Hubli, Hyderabad, Jaipur, Jodhpur, Kolkata, Lucknow, Ludhiana, Madurai, Meerut, Mumbai, Mysore, Nagpur, Patna, Pune, Siliguri, Surat, Thiruvananthapuram, Varanasi, Vijayawada, Visakhapatnam
*PWD: People with Diabetes

Contact for more information
Nikita Thawarkar | 7304930643 | nikita.thawarkar@usv.in

In T2DM Uncontrolled on DPP4i + Metformin,SGLT2i + Metformin, SGLT2i + DPP4i,

Uptitrate with

UDAPA-Trio

Dapagliflozin 10 mg + Sitagliptin 100 mg + Metformin 500 mg XR

UDAPA-Trio Forte

Dapagliflozin 10 mg + Sitagliptin 100 mg + Metformin 1000 mg XR

IMPROVED iCARE STARTS WITH U

Cardio Benefits | **A**1C Control | **R**enal Benefits | **E**nsures Adherence

Abridged Prescribing Information

Indication: It is indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus.
Dosage and Administration: The recommended dose is one tablet daily. Each tablet contains a fixed dose of dapagliflozin, Sitagliptin and Metformin Hydrochloride.
Adverse Reactions: Most common adverse reactions reported are: Dapagliflozin- Female genital mycotic infections, nasopharyngitis, and urinary tract infections. Sitagliptin- Upper respiratory tract infection, nasopharyngitis and headache. Metformin- Diarrhea, nausea/vomiting, flatulence, asthenia, indigestion, abdominal discomfort, and headache.
Warnings and Precautions: Dapagliflozin: Volume depletion; Ketoacidosis in Patients with Diabetes Mellitus; Urosepsis and Pyelonephritis; Hypoglycaemia; Genital Mycotic infections
Sitagliptin: General- Sitagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Acute pancreatitis: Hypoglycaemia when used in combination with other anti-hyperglycaemic medicinal product; Renal impairment; Hypersensitivity reactions including anaphylaxis, angioedema, and exfoliative skin conditions- Stevens-Johnson syndrome; Bullous pemphigoid. Metformin Hydrochloride: Lactic acidosis; In case of dehydration (severe diarrhoea or vomiting, fever or reduced fluid intake), metformin should be temporarily discontinued and contact with a healthcare professional is recommended.
Contraindications: Hypersensitivity to the active substance of Dapagliflozin, Sitagliptin & Metformin or to any of the excipients listed. Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis). Diabetic pre-coma; Severe renal failure (eGFR< 30mL/min); Acute conditions with the potential to alter renal function such as: Dehydration, Severe Infection, Shock; Acute or chronic disease which may cause tissue hypoxia such as: Cardiac or respiratory failure, Recent myocardial Infarction, Shock, Hepatic Impairment, Acute Alcohol Intoxication, alcoholism
Use in a special population: Pregnant Women: Due to lack of human data, drug should not be used during pregnancy. Lactating Women: It should not be used during breastfeeding. Paediatric Patients: The safety and efficacy of drug has not yet been established. No data are available. Geriatric Patients: In Patients > 65 years, it should be used with caution as age increases.

Additional information is available on request.
Last updated: January 03, 2023

USV | Corvette

In case of any adverse events, kindly contact pv@usv.in For the use of registered medical practitioner, hospital or laboratory

In Uncontrolled Obese T2DM,

START with,

Glycomet®-GP 1 FORTE

Metformin Hydrochloride 1000 mg SR + Glimepiride 1 mg

Glycomet®-GP 2 FORTE

Metformin Hydrochloride 1000 mg SR + Glimepiride 2 mg

Glycomet®-GP 3/850

Metformin Hydrochloride 850 mg SR + Glimepiride 3 mg

January 2023[1]

ESC*
European Society of Cardiology

Long term continuous usage of High Dose Glimepiride:

Inhibits sEH → Increases EET

Greater Cardiovascular Protection

Meta analysis of 21 well established trials[2]

5% Reduction of Weight Vs Baseline Weight[2]

100% Availability

20-50%# Affordable vs other brands

Appropriate to add along with Newer AHAs

1. Glimepiride use is associated with reduced cardiovascular mortality in patients with type 2 diabetes and chronic heart failure, a prospective cohort study | European Journal of Preventive Cardiology | Oxfont Academic (oup.com) 2. Ther Adv Endocrinol Metab 2020. Vol 11:1-12 DOI: 10. 1177/2042018820926000. # Data on file * As compared to non-glimepiride group
EET: Epoxyeicosatrienoic acid; sEH: soluble Epoxide Hydrolase; AHAs: antihyperglycemic agents; T2DM: Type 2 Diabetes Mellitus

Prescribing Information

Information: Metformin hydrochloride (as prolonged release) and glimepiride tablets. Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/850/ Glycomet-GP 2/ Glycomet-GP 2/850/ Glycomet-GP 3/ Glycomet-GP 3/850/ Glycomet-GP 4/ Glycomet-GP 4/850/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte Abridged Prescribing Information **Composition:** Glycomet GP 0.5mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500mg and glimepiride IP 0.5mg.• Glycomet GP 0.5 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 0.5mg.• Glycomet GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. • Glycomet GP 1/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. • Glycomet GP 2: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 2 mg. • Glycomet GP 2/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 2 mg.• Glycomet GP 3: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 3 mg. • Glycomet GP 3/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 3 mg. • Glycomet GP 4: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 4 mg. • Glycomet GP 4/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 4 mg. •Glycomet GP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 1mg. • Glycomet GP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 2mg. • Glycomet GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 3mg. • Glycomet GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP mg. **Indication:** For the management of patients with type 2 diabetes mellitus when diet, exercise and single agent (glimepiride or metformin alone) do not result in adequate glycaemic control. **Dosage and Administration:** The recommended dose is one tablet daily during breakfast or the first main meal. Each tablet contains a fixed dose of glimepiride and Metformin Hydrochloride. The highest recommended dose per day should be 8 mg of glimepiride and 2000mg of metformin. Due to prolonged release formulation, the tablet must be swallowed whole and not crushed or chewed. **Adverse Reactions:** For Glimepiride: hypoglycaemia may occur, which may sometimes be prolonged. Occasionally, gastrointestinal (GI) symptoms such as nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhea may occur. Hepatitis, elevation of liver enzymes, cholestasis and jaundice may occur; allergic reactions or pseudo allergic reactions may occur occasionally. For Metformin: GI symptoms such as nausea, vomiting, diarrhea, abdominal pain, and loss of appetite are common during initiation of therapy and may resolve spontaneously in most cases. Metallic taste, mild erythema, decrease in Vit B12 absorption, very rarely lactic acidosis, Hemolytic anemia, Reduction of thyrotropin level in patients with hypothyroidism, Hypomagnesemia in the context of diarrhea, Encephalopathy, Photosensitivity, hepatobiliary disorders. **Warnings and Precautions:** For Glimepiride: Patient should be advised to report promptly exceptional stress situations (e.g., trauma, surgery, febrile infections), blood glucose regulation may deteriorate, and a temporary change to insulin may be necessary to maintain good metabolic control. Metformin Hydrochloride may lead to Lactic acidosis; in such cases metformin should be temporarily discontinued and contact with a healthcare professional is recommended. Sulfonylureas have an increased risk of hypoglycaemia. Long-term treatment with metformin may lead to peripheral neuropathy because of decrease in vitamin B12 serum levels. Monitoring of the vitamin B12 level is recommended. Overweight patients should continue their energy-restricted diet, usual laboratory tests for diabetes monitoring should be performed regularly. **Contraindications:** Hypersensitivity to the active substance of glimepiride & Metformin or to any of the excipients listed. Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis, diabetic pre-coma). Severe renal failure (GFR<30ml/min). In pregnant women. In lactating women Acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents); acute or chronic disease which may cause tissue hypoxia (cardiac or respiratory failure, recent myocardial infarction, shock); hepatic insufficiency; acute alcohol intoxication; alcoholism. **Use in a special population:** Pregnant Women: Due to a lack of human data, drugs should not be used during pregnancy. Lactating Women: It should not be used during breastfeeding. Pediatric Patients: The safety and efficacy of drugs has not yet been established. Renal impairment: A GFR should be assessed before initiation of treatment with metformin containing products and at least annually thereafter. In patients at increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g. every 3-6 months.

Additional information is available on request.

Last updated: March 13, 2023

*In case of any adverse events, kindly contact: pv@usv.in

For the use of registered medical practitioner, hospital or laboratory.*

USV Private Limited Corvette Team

Anvind Vithal Gandhi Chowk, B. S. D. Marg, Govandi, Mumbai - 400 088. | Tel.: 91-22-2556 4048 | Fax: 91-22-2558 4025 | www.usvindia.com

Oral Antidiabetic Medications and Gut Microbiome

Dr. Manish Agarwal

MD, PhD, PGDDM, FACP (USA), Diploma in Endocrinology

Consultant Diabetologist and Metabolic Physician, Medilink Hospital, Ahmedabad

The therapeutic efficacy and potential side effects following the use of antidiabetic drugs is influenced by resident microbiota and the presence of certain genera/species could influence individual's response to drugs and their side effects. Orally administered drugs interact with millions of resident microbes in the gastrointestinal tract. Understanding this bidirectional interaction and its effect on clinical outcomes may pave the way for the development of innovative strategies for diabetes treatment.

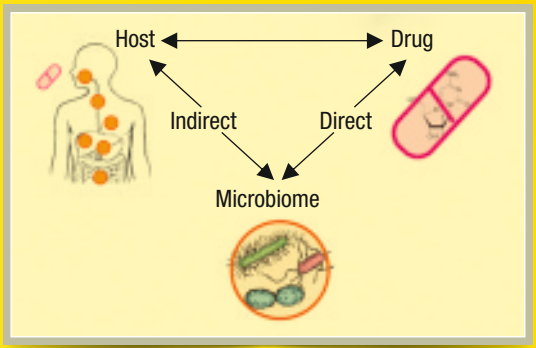
Oral antidiabetic drugs and their effect on gut microbiota composition

Oral antidiabetic drugs	Effects
Metformin	Metformin exerts antihyperglycemic action by modulation of the gut microbiota. It is found to be associated with increased abundance of short-chain fatty acids (SCFA)-producing gut microbiota such as *Butyrivibrio, Bifidobacterium bifidum,* and *Megasphaera* that improve metabolic homeostasis, insulin sensitivity, and energy expenditure. It also increases abundance of *Akkermansia muciniphila* that protects the mucus layer and decreases the permeability of the gut barrier. It also increases abundance of *Escherichia* species that are related to the gastrointestinal side effects. As a result, a small percentage of individuals with diabetes may discontinue metformin because of intolerance to these side effects.
Sulfonylurea and glinide	Sulfonylureas and glinides stimulate insulin secretion from pancreatic β-cells, lowering blood glucose levels. A study on individuals with type 2 diabetes (T2DM) found that three months of glipizide treatment had no significant impact on gut microbiota composition or plasma bile acid levels. No human studies on the effect of glinide on gut microbiota have been reported yet.
α-glucosidase inhibitors	α-glucosidase inhibitors reduce postprandial hyperglycemia by inhibiting carbohydrate hydrolysis and may have beneficial effects on glycemic control via gut microbiota. In individuals with T2DM treated with α-glucosidase inhibitors, a higher abundance of beneficial *Bifidobacterium* and *Lactobacillus* (SCFA-producing bacteria), lower levels of endotoxic and inflammatory lipopolysaccharides (LPS) was observed. A decrease in pro-inflammatory *Bacteroides* has also been reported in another study. Furthermore, α-glucosidase inhibitors administration has also shown a decrease in *Firmicutes* to *Bacteroidetes* ratio improving blood glucose and lipid metabolism.
Glucagon like peptide (GLP -1)	GLP-1, an incretin hormone secreted by intestinal L cells, regulated glucose homeostasis and satiety via gut microbiota. GLP-1 has shown to increase beneficial SCFA-producing bacteria such as *Bacteroides,* Lachnospiraceae, *Bifidobacterium,* and gut barrier strengthening *Akkermansia muciniphila* and decrease pro-inflammatory *proteobacteria.*

Oral antidiabetic drug	Effects
Thiazolidinedione (TZDs) and Dipeptidyl peptidase 4 (DPP4) inhibitors	DPP-4 inhibitors reduce blood glucose blocking the degradation of GLP-1 and restore the gut microbiota composition by increasing the abundance of *Bacteroidetes*. No human studies have been published regarding the TZD effects on the gut microbiota, but studies in mice have shown they increase the relative abundance of gut strengthening *Akkermansia*.
Sodium glucose co-transporter 2 (SGLT-2) inhibitor	Numerous investigations have observed gut microbiota composition to be unaffected by SGLT-2 inhibitors. One study found they increased the gut strengthening *Akkermansia muciniphila* and decreased the ratio of *Firmicutes* to *Bacteroidetes*. More research is needed in this area.

Key points

- Antidiabetic drugs interact with millions of resident microbes in the gastrointestinal tract.
- Different antidiabetic drugs have varying effects on the composition of gut microbiota. Therapeutic efficacy and potential side effects following the use of antidiabetic drugs is influenced by resident microbiota.
- Gut microbiota composition may in the future serve as a biomarker to choose the best regimen to treat T2DM.



Resources:

1. Hung W-W, Hung W-C. How Gut Microbiota relate to the oral antidiabetic treatment of type 2 diabetes. *Medicine in Microecology*. 2020;3:100007. doi:10.1016/j.medmic.2020.100007.
2. Crudele L, Gadaleta RM, Cariello M, Moschetta A. Gut microbiota in the pathogenesis and therapeutic approaches of diabetes. *EBioMedicine*. 2023;97:104821. doi:10.1016/j.ebiom.2023.104821

Gut Microbiota and Complications of Diabetes

Dr. Devi Gayathri Palanivel

MBBS, DNB (Internal Medicine), PG Diploma in Diabetes

Consultant Physician and Diabetologist, Royal Care Super Speciality Hospital, Coimbatore

Uncontrolled diabetes can cause blindness, kidney impairment, stroke, heart attack, and limb amputation. The gut microbiota plays a role in the progression of diabetes-associated complications such as nephropathy, retinopathy, neuropathy, cerebrovascular disease, peripheral vascular disease, and coronary heart disease. The table below discusses alterations in gut microbiota in diabetes-associated complications and available evidence on probiotic administration. More clinical trials evaluating the efficacy of probiotic/synbiotic administration, and their therapeutic potential are required.

Endocrine disorders leading to diabetes

Diabetes complications	Effect of gut microbiota on complications
Diabetic retinopathy	Diabetic retinopathy, stemming from unmanaged diabetes, poses a risk of eventual blindness. The ocular surface microbiota primarily comprises *Proteobacteria*, *Actinobacteria*, and *Firmicutes*, while the internal eye compartment remains sterile. Studies have linked an imbalance in gut microbiota, characterized by decreased *Bacteroidetes* and *Actinobacteria*, with diabetic retinopathy. Furthermore, alterations in ocular and gut microbiota composition, including decreases in *Mucoromycota* and Pasteurellaceae, along with elevated levels of microbiota-derived trimethylamine N-oxide, are associated with the severity of diabetic retinopathy, highlighting the interplay between microbiota and disease progression. In preclinical models of diabetic retinopathy, the administration of probiotics has demonstrated the potential to positively influence the profile of gut microbiota.
Diabetic nephropathy	In both animal and human studies in chronic kidney disease, there's a notable decrease in beneficial bacteria like *Bifidobacterium, Bacteroides,* and *Lactobacillus*, alongside an increase in potentially harmful microbes such as *Parabacteroides* and *Enterococcus*. This imbalance, marked by reduced antiinflammatory bacteria, is associated with systemic inflammation and compromised intestinal barrier integrity. Probiotic interventions, including combinations like *Lactobacillus acidophilus, Streptococcus thermophilus,* and *Bifidobacterium longum,* have shown promise in reducing urea nitrogen and uric acid levels, suggesting a potential avenue for managing chronic kidney disease and its complications.
Diabetic neuropathy	Altered gut microbiota, with increased *Firmicutes* and *Actinobacteria* and decreased *Bacteroidetes*, is associated with diabetic neuropathy. Specific genera changes include reductions in *Bacteroides* and *Faecalibacterium* and increases in *Escherichia-Shigella, Lachnoclostridium, Blautia, Megasphaera,* and *Ruminococcus torques*. Elevated *Megasphaera* levels correlate with insulin resistance, possibly contributing to neuropathy onset. Interventions like Bifidobacteria and *Lactobacillus* supplementation show promise in improving insulin resistance. Further research is needed to understand gut microbiota's role in neuropathy, for potential of probiotic or synbiotic supplements.

Diabetes complications	Effect of gut microbiota on complications
Cerebrovascular disease	Acute ischemic stroke triggers changes in gut microbiota, characterized by elevated *Lactobacillus ruminis* and decreased *Lactobacillus sakei.* This dysbiosis contributes to impair neuroinflammatory processes, worsening the condition. Additionally, elevated trimethylamine-N-oxide (TMAO) levels found in stroke patients are correlated with heightened inflammation. Preclinical studies exploring probiotic supplementation to alleviate gut dysbiosis linked with cerebrovascular disease have demonstrated promising outcomes. One study found probiotic administration to help with a notable reduction in oxidative stress marker malondialdehyde and inflammatory cytokine TNF-α levels within the ischemic brain tissue.
Coronary heart disease	Gut microbiota dysbiosis is linked to coronary artery disease, hypertension, and heart failure. Studies indicate a higher frequency of coronary artery disease with a low proportion of intestinal bacteria. Gut microbiota influences coronary artery disease development via metabolite production of bile acids, coprostanol, and TMAO, with TMAO strongly associated with disease risk. Probiotics in coronary artery disease patients reduce blood lipids, with *Lactobacillus plantarum 299* shown to improve endothelial function and decrease inflammation and a supplement containing *Bifidobacterium bifidum, Lactobacillus casei,* and *Lactobacillus acidophilus* has shown to improve glycemic control, increase HDL-cholesterol, and reducing oxidative stress biomarkers in coronary artery disease patients.
Peripheral vascular disease	Beneficial effects of probiotic supplementation on wound healing in diabetes has been observed. Individuals with diabetic foot disease who underwent a 12-week probiotic regimen *(Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus fermentum*, and *Bifidobacterium bifidum* (2×10^9 CFU/g)) improved QUICKI (quantitative insulin-sensitivity check index) indicator, plasma glucose, serum insulin, and also demonstrated a decrease in the ulcer's length, width, and thickness.

Key points

- The gut microbiota plays a role in the progression of diabetes-associated complications such as nephropathy, retinopathy, neuropathy, cerebrovascular disease, peripheral vascular disease, and coronary heart disease.
- Positive impact of probiotic administration is observed diabetes associated complications. More clinical trials are required to provide a therapeutic recommendation.

Resources:

1. Iatcu CO, Steen A, Covasa M. Gut Microbiota and Complications of Type-2 Diabetes. *Nutrients.* 2021;14(1):166. Published 2021 Dec 30. doi:10.3390/nu14010166.

Role of Gut Microbiota in Type 1 Diabetes Pathophysiology

Dr. Vedavati Purandare

MBBS, MD (Medicine), PhD

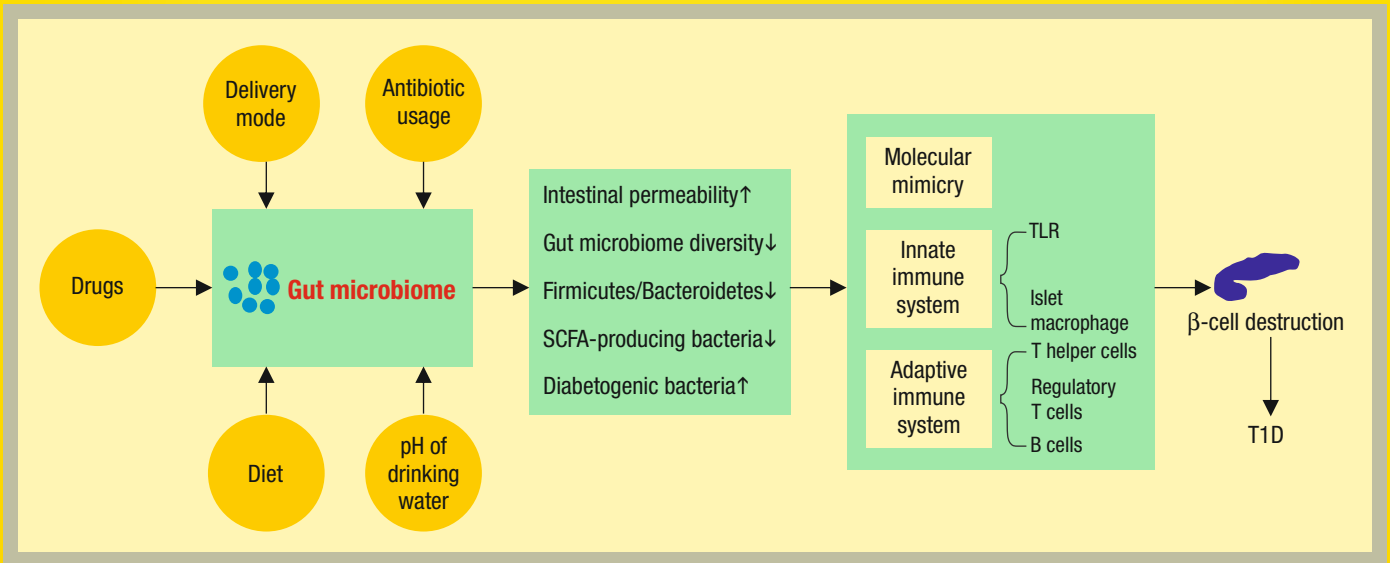
Clinical Head, Consultant Physician and Diabetologist, Chellaram Diabetes Institute, Pune

Type 1 diabetes (T1D) is an autoimmune disease governed by genetic, epigenetic, and environmental factors. Dysbiosis, or the disruption of the normal gut microbiota has been identified as one of the environmental variables linked to the onset of autoimmune conditions such as T1D and other inflammatory illnesses.

Role in pathogenesis

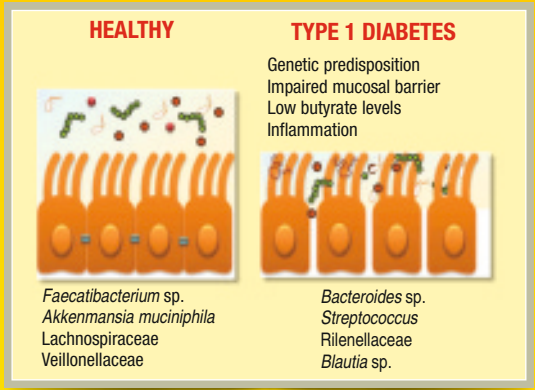
The gut microbiota is active, varied, and abundant. Given the increasing evidence of T1D, determining the role of gut microbiota in the pathophysiology is important. Environmental factors such as diet, antibiotic use, lifestyle influence the gut microbiota. The exact mechanism is not completely known, however, it is known that the gut microbiota can influence intestinal permeability, modulate the innate and adaptive immune systems, and act as a molecular mimic thus playing a role in T1D pathogenesis (as shown in the figure).

Immune system homeostasis and the integrity of the intestinal barrier depend on the gut microbiome. When gut dysbiosis occurs in genetically vulnerable individuals, it increases intestinal permeability causing microbial antigens to dysregulate innate and adaptive immune systems. These antigens may be taken up by antigen presenting cells (APCs) and may present them to auto reactive T lymphocytes, consequently leading to pancreatic beta cell death and T1D. Molecular mimicry is another potential way by which these translocated microbial antigens cause the onset of diabetes. Certain microbial antigens are homologous to the islet self-antigen, which can lead to T-cell cross-reactivity and the eventual loss of islet beta cells.



Abbreviations: SCFA: Short-chain fatty acid; T1D: Type 1 diabetes; TLR: Toll-like receptors

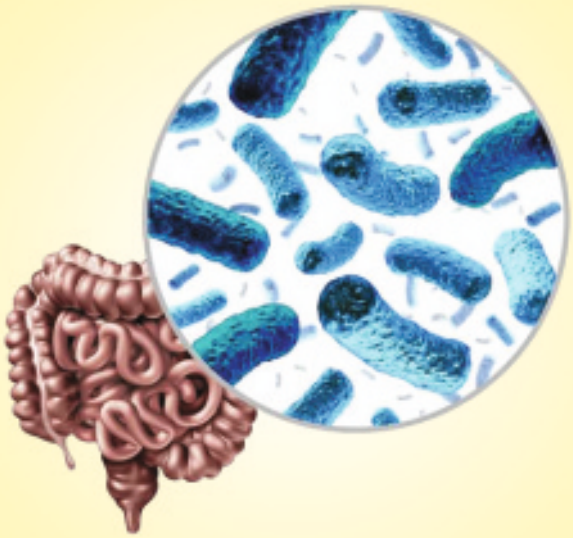
Reduced diversity of the gut microbiome has been reported before the onset of T1D. T1D children were observed to have decreased abundance of two dominant *Bifidobacterium* species and more of the phylum Bacteroidetes when compared to healthy children in a study. T1D children are also found to have increased intestinal permeability associated with altered gut microbiota. Accumulating evidence suggests a significant role of intestinal microbiota influencing immunological homeostasis and/or gut permeability in the etiology of T1D. Thus, preserving a healthy gut microbiome should be included among T1D preventive and treatment strategies.



Resources:

1. Zhou H, Sun L, Zhang S, *et al.* Evaluating the Causal Role of Gut Microbiota in Type 1 Diabetes and Its Possible Pathogenic Mechanisms. *Front Endocrinol (Lausanne).* 2020;11:125. doi:10.3389/fendo.2020.00125
2. Del Chierico F, Rapini N, Deodati A, *et al.* Pathophysiology of Type 1 Diabetes and Gut Microbiota Role. *Int J Mol Sci.* 2022;23(23):14650. doi:10.3390/ijms232314650
3. Zheng P, Li Z, Zhou Z. Gut microbiome in type 1 diabetes: A comprehensive review. *Diabetes Metab Res Rev.* 2018;34(7):e3043. doi:10.1002/dmrr.3043.
4. De Goffau MC, Fuentes S, van den Bogert B, *et al.* Aberrant gut microbiota composition at the onset of type 1 diabetes in young children. *Diabetologia.* 2014;57(8):1569-1577. doi:10.1007/s00125-014-3274-0
5. Harbison JE, Roth-Schulze AJ, Giles LC, *et al.* Gut microbiome dysbiosis and increased intestinal permeability in children with islet autoimmunity and type 1 diabetes: A prospective cohort study. *Pediatr Diabetes.* 2019;20(5):574-583. doi:10.1111/pedi.12865.
6. Pircalabioru GG, Picu A, Petcu L, P *et al.* The Intricate Relationship between Diabetes, Diet and the Gut Microbiota [Internet]. Pathophysiology - Altered Physiological States. InTech; 2018. Available from: http://dx.doi.org/10.5772/intechopen.70602

ROLE OF GUT MICROBIOTA IN TYPE 1 DIABETES



Diabetes and Gut Friendly Foods

Dr. Saurabh Agarwal

MBBS, MD (Manipal), FIDM (UK), FAGE, CCID (UK), CCEBDM

Consultant Physician and Diabetologist,
Swasthyam Medical Clinic, Lucknow

The gut microbiota, a diverse ecosystem in the gastrointestinal tract, affects human health and is linked to various diseases including type 2 diabetes mellitus (T2DM). The following gut friendly foods that can be advised to individuals with diabetes.

Diverse foods for a diverse microbiome

Include a variety of fiber-rich foods like legumes, beans, fruits and vegetables for a diverse microbiome, fostering the growth of beneficial Bifidobacteria.

Consume fermented foods

Include fermented foods like yogurt, kimchi, kefir, kombucha, black carrot kanji, fermented rice (panta bhaat), and buttermilk, for beneficial *Lactobacilli* and reducing harmful gut bacteria.

Fuel healthy bacteria with prebiotics

Consume prebiotic-rich foods such as raw banana, onion, leeks, jackfruit seeds, garlic, prunes/raisins (in moderation), pear, and apples to stimulate the growth of beneficial bacteria.

Whole grains for gut well-being

Include whole grains such as millets, barley, broken wheat, rolled oats/steel cut oats into diet to provide fiber, and functional ingredients like beta-glucan that promote healthy gut.

Polyphenol-rich foods for gut health

Include polyphenol-rich foods apple, grapes, berries, onion, olives, and olive oil (in moderation), legumes, and whole grains to stimulate the growth of healthy bacteria.

Including these gut-friendly foods in will help maintain gut health, reduce risk of complications, and ensure overall well-being in individuals with diabetes.

Key points

Gut friendly foods for individuals with diabetes- yogurt, buttermilk, whole grains, millets, broken wheat, barley, oats, beans, legumes, vegetables, onion, garlic fruits especially apple, grapes, berries, banana, and prunes/raisins (in moderation).

Resources:

1. Zhou Z, Sun B, Yu D and Zhu C. Gut Microbiota: An Important Player in Type 2 Diabetes Mellitus. *Front. Cell. Infect. Microbiol.* 2022, 12:834485. doi: 10.3389/fcimb.2022.834485
2. Pires C. Superfoods for Type 2 Diabetes: A Narrative Review and Proposal for New International Recommendations. *Medicina (Kaunas).* 2023;59(7):1184. doi:10.3390/medicina59071184.
3. P NPV, Joye IJ. Dietary Fibre from Whole Grains and Their Benefits on Metabolic Health. *Nutrients.* 2020;12(10):3045. doi:10.3390/nu12103045.
4. Dreher ML. Whole Fruits and Fruit Fiber Emerging Health Effects. *Nutrients.* 2018;10(12):1833. doi:10.3390/nu10121833.
5. Guasch-Ferré M, Merino J, Sun Q, *et.al.* Dietary Polyphenols, Mediterranean Diet, Prediabetes, and Type 2 Diabetes: A Narrative Review of the Evidence. *Oxid Med Cell Longev.* 2017;2017:6723931. doi:10.1155/2017/6723931.

Frequently Asked Questions on Diabetes and Gut Health

Dr. Ega Lakshman Kumar

MD (Gen Medicine), DM (Endocrinology)

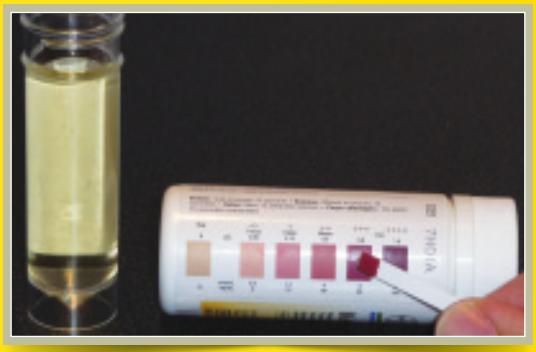
Consultant Endocrinologist, Padmakshi Polyclinic, Warangal

1. My 7-year-old child was diagnosed with type 1 diabetes mellitus a year ago. So far we have been able to keep her blood glucose levels stable. A few weeks ago she had a stomach infection and suffered from diarrhea. This caused her sugar levels to spike drastically. We were very confused and were unaware on how to manage the same. Please guide us on how to manage her glucose levels when she is sick.

Ans. People with diabetes, like everyone else, are susceptible to illness despite their best efforts to be healthy. Therefore, it is important to be prepared and know what to do if you become ill.

Here are few key points to remember during sick days

- **S (Sugar):** Check your blood sugar often (at least 4 hourly, more frequently if needed)
- **I (Insulin):** Do not stop insulin. Insulin dose may need to be increased or decreased, based on blood sugar level and food intake.
- **C (Carbohydrates):** Stick to your regular diet, including soft, carb-rich foods if eating is challenging. Stay hydrated with fluids. For high blood sugar, choose clear soups, lemon water, buttermilk, and for low blood sugar, go for carb-containing foods like fruit juices, lemon water with sugar, glucose water, etc. Aim for 15 g of carbs every 3-4 hours.
- **K (Check for ketones):** Regularly monitor for ketones to prevent diabetic ketoacidosis (DKA). Check urine or blood ketones every 4 hours, especially if blood sugar is consistently high (>250 mg/dL) with symptoms like vomiting or stomach pain. If ketones are present, consider rapid-acting insulin and contact your doctor urgently. Stay hydrated to flush out ketones.



2. I am a 62-year-old individual with type 2 diabetes mellitus for the past eight years. Lately, I have been suffering from gastric issues, especially bloating and acidity, and I am unable to understand why. I am not entirely in favor of taking medications for the same. Are there any dietary tips that I can follow to reduce the same?

Ans. Bloating is a perception that the abdomen is larger than usual despite the physical size not increasing. The sensation arises from intestinal gas, which can create the feeling of abdominal distension.

Bloating causes

- Swallowing air during habits like gum chewing, talking while eating
- Consuming bulky foods such as lettuce, cabbage, and dense breads

- Ingesting air with beverages and certain foods like carbonated drinks
- Certain medications can cause bloating. If it persists, discuss it with your doctor.

Tips to reduce bloating

- Chew food thoroughly and eat slowly. Have smaller, more frequent meals
- Avoid behaviors that introduce air, like gulping foods or using straws
- Ensure proper denture fit
- Engage in regular physical activity
- Consider natural remedies like peppermint or fennel/chamomile tea

Additional tips

- Keep a food record to identify triggering foods or behaviors
- Seek medical attention if symptoms persist or worsen, especially with accompanying issues like weight loss, diarrhea, vomiting, or heartburn

3. I am a 49-year-old individual with diabetes. I was facing severe constipation issues, and my cholesterol levels were elevated. I was advised to start taking Psyllium Husk (Isabgol) for the same. I am afraid that it will be addictive, and over usage may have some side-effects after long-term use. Kindly advise about the same.

Ans. Psyllium Husk acts as a bulking agent and forms a gel-like mass, promoting efficient waste elimination by drawing water from the colon. Unlike various other laxatives, Psyllium Husk is gentle and not addictive. However, one must be mindful of certain factors while consuming it, such as:

- Psyllium Husk, if not taken with sufficient fluid, may cause blockages in the throat and esophagus while swallowing. It can also cause constipation if taken with insufficient fluid. Thus, make sure to have enough water with your psyllium as well as additional water afterwards if needed to avoid chocking.
- To avoid potential drug interactions, consume Isabgol a few hours after medications.
- Long-term use may hinder the absorption of nutrients like iron, zinc, copper, magnesium, vitamin B_{12}, and carbohydrates.
- Some individuals find relief from irritable bowel syndrome (IBS) symptoms, such as constipation, through the consumption of soluble fiber like psyllium seed husk.

Thus, while Psyllium Husk is safe to use, one must also consider other factors such as time, amount and water consumption to avail the best benefits.

Did You Know Our Traditional Indian Food - Panta Bhaat is Good for Gut Health?

Panta Bhaat, also known as Poita bhaat/Pakhala/Bore bassi/Geel bhaat/Pazhaya soru/Pazhan kanji is a popular traditional dish in India and mainly consumed by people in West Bengal, Assam, Odisha, Chhattisgarh, Bihar, Tamil Nadu, and Kerala. It is consumed mostly for breakfast and lunch and especially on the day of Pahela Baishakh or Bengali New Year.

Rice and water are the main ingredients. It is a prepared by soaking rice, generally leftover, in water overnight for fermentation. Traditionally served in the morning with salt, onion, chilli, papad/pickle/lemon and mashed potatoes or "Alu Makha". Some also eat Dahi (Indian curd), green vegetables, lentils, and fish along.

This fermented rice is a hydrating meal. It is the optimal choice of food for a summer afternoon that not only helps in cooling the body but also offers relief from heartburn and ulcers. The fermentation process fosters the growth of beneficial bacteria having probiotic properties. It helps restore healthy intestinal microflora, regulates bowel movement, and also helps prevent gastrointestinal disorders such as duodenal ulcers, infectious ulcerative colitis, Crohn's disease, etc. The fermentation process also increases Vitamin K and B-complex levels.

Fermented foods made from cereals are becoming more and more popular, due to their gut-friendly nature and increasing evidence on the role of gut microflora in prevention and management of diseases.

Panta Bhaat belonging to our traditional Indian cuisine is a gut friendly and nutritious meal perfect for hot summer days.

Resources:

1. Ray, Mousumi, *et al.* Folk to functional: An explorative overview of rice-based fermented foods and beverages in India. *Journal of Ethnic Foods.* (2016). 3. 10.1016/j.jef.2016.02.002.
2. Tsafrakidou P, Michaelidou AM, G Biliaderis C. Fermented Cereal-based Products: Nutritional Aspects, Possible Impact on Gut Microbiota and Health Implications. *Foods.* 2020;9(6):734. Published 2020 Jun 3. doi:10.3390/foods9060734.

Dia-Games

True or False

1. Gut microbiota dysbiosis is not linked to chronic kidney disease.
2. Fiber-rich foods like legumes, beans, and fruits can increase the growth of beneficial Bifidobacteria.
3. Hyperglycemia in diabetes is a known cause of gastroparesis affecting the gastric emptying rate.
4. Individuals with gastroparesis have no dietary restrictions.
5. Domperidone is a prokinetic agent, that promotes stomach emptying by blocking dopamine receptors in the brain and increases motility in the gastrointestinal tract, prescribed for gastroparesis.
6. Low fat and high fiber diet is advised for individuals with gastroparesis.
7. Smoking and alcohol exacerbate gastroparesis symptoms.

Answers

1. False
2. True
3. True
4. False
5. True
6. False
7. True

NOTES

In Newly Diagnosed & Young T2DM,

Start Early with

Glycomet®-GP 0.5

Metformin Hydrochloride 500 mg SR + Glimepiride 0.5 mg

Glycomet®-GP 0.5 FORTE

Metformin Hydrochloride 1000 mg SR + Glimepiride 0.5 mg

Recent Glycomet®-GP Real World SWITCH STUDY 2023' Patients[1]

94% of **T2DM patients Switched** from DPP4i with or without Metformin combination to Low Dose Glimepiride + Metformin

Resulted in

significant **HbA1c reduction** of **1.65%**

Global Innovator with 100% Accessibility

Lesser Risk of Hypoglycemia

Lower Risk of Weight Gain[2]

T2DM: Type 2 Diabetes Mellitus; **HbA1c**: Hemoglobin A1c.

1. SWITCH STUDY (*Data on file*). 2. Diabetes Obes Metab 2017; 19:1180-1192; Endocrine Journal 2014; 61 (12), 1163-1170.

Information

Metformin hydrochloride (as prolonged release) and glimepiride tablets.

Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/850/ Glycomet-GP 2/ Glycomet-GP 2/850/ Glycomet-GP 3/ Glycomet-GP 3/850/ Glycomet-GP 4/ Glycomet-GP 4/850/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte.

Abridged Prescribing Information

Composition: • Glycomet GP 0.5 mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 0.5 mg. • Glycomet GP 0.5 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP 0.5 mg. • Glycomet GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. • Glycomet GP 1/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. • Glycomet GP 2: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 2 mg. • Glycomet GP 2/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 2 mg. • Glycomet GP 3: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 3 mg. • Glycomet GP 3/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 3 mg. • Glycomet GP 4: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 4 mg. • Glycomet GP 4/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 4 mg. • Glycomet SP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP 1 mg. • Glycomet SP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP 2 mg. • Glycomet GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP 3 mg. • Glycomet GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000 mg and glimepiride IP mg. **Indications:** Glycomet GP is indicated for the management of patients with type 2 diabetes mellitus (T2DM) when diet, exercise and single agent (metformin hydrochloride or glimepiride alone) do not result in adequate glycemic control. **Dosage and Administration:** Dosage of Glycomet GP should be individualized on the basis of effectiveness and tolerability while not exceeding the maximum recommended daily dose of glimepiride 8mg and metformin 2000 mg. Initial dose: 1 tablet of Glycomet GP should be administered once daily during breakfast or with the first main meal. Do not crush or chew the tablet. In several cases the tablet may remain intact during transit through the gastrointestinal (GI) tract and will be eliminated in feces as hydrated matrix (ghost matrix). Patients should be advised that this is normal as all drug components have already been released during GI transit. **Contraindications:** In patients hypersensitive to glimepiride, other sulfonylureas, other sulfonamides, metformin or any of the excipients of Glycomet GP, pregnancy and lactation; diabetic ketoacidosis, diabetic pre-coma, in patients with eGFR<30 ml/min/ 1.73 m², acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents), acute or chronic disease which may cause tissue hypoxia (myocardial infarction, shock, cardiac/respiratory failure), hepatic insufficiency, acute alcohol intoxication, alcoholism. **Warnings:** Keep out of reach of children. Patient should be advised to report promptly exceptional stress situations (e.g. trauma, surgery, febrile infections). Blood glucose regulation may deteriorate and a temporary change to insulin may be necessary to maintain good metabolic control. In case of lactic acidosis, patient should be hospitalized immediately. **Precautions:** In the initial weeks of treatment, the risk of hypoglycemia may be increased and necessitates especially careful monitoring. Serum creatinine level should be determined before initiating treatment and regularly thereafter, at least annually in patients with normal renal function. Intravascular contrast studies with iodinated materials can lead to acute alteration of renal function. In patients in whom such study is planned, Glycomet GP should be temporarily discontinued at the time of or prior to the procedure, and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal. Use of Glycomet GP should be discontinued 48 hours before any surgical procedure. **Adverse reactions:** For glimepiride – hypoglycaemia; temporary visual impairment; GI symptoms like nausea, vomiting, abdominal pain, diarrhoea may occur; increased liver enzymes; cholestasis and jaundice may occur; allergic reactions may occur occasionally. For metformin – GI symptoms like nausea, vomiting, abdominal pain or discomfort may occur.

In case of any adverse events, kindly contact: pv@usv.in
For the use of registered medical practitioner, hospital or laboratory.

USV Private Limited

Ambedkar Vithal Gandhi Chowk, B. S. D. Marg, Govandi, Mumbai - 400 088. | Tel.: 91-22-2556 4048 | Fax: 91-22-2556 4025 | www.usvindia.com

Beat Diabetes
Win Life

For screening people with High & Moderate Risk of Diabetes

Indian Diabetes Risk Score

Share this simple test with your family & Friends

Users can share it with their family & friends

Video on Suggestive Lifestyle Interventions to minimise risks - for each category

12 Languages

An awareness initiative by USV

USV

is making

Indian Diabetes Risk Score

Accessible to Every INDIAN

For Screening people with High & Moderate Risk of Diabetes

TO KNOW YOUR RISK OF DIABETES SCAN HERE

Beat Diabetes Win Life

USV

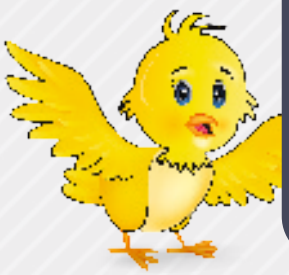
is making

Indian Diabetes Risk Score

Accessible to Every INDIAN

For Screening people with High & Moderate Risk of Diabetes

TO KNOW YOUR RISK OF DIABETES SCAN HERE



Beat Diabetes Win Life

USV

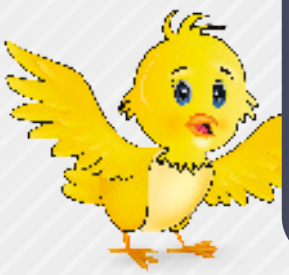
is making

Indian Diabetes Risk Score

Accessible to Every INDIAN

For Screening people with High & Moderate Risk of Diabetes

TO KNOW YOUR RISK OF DIABETES SCAN HERE

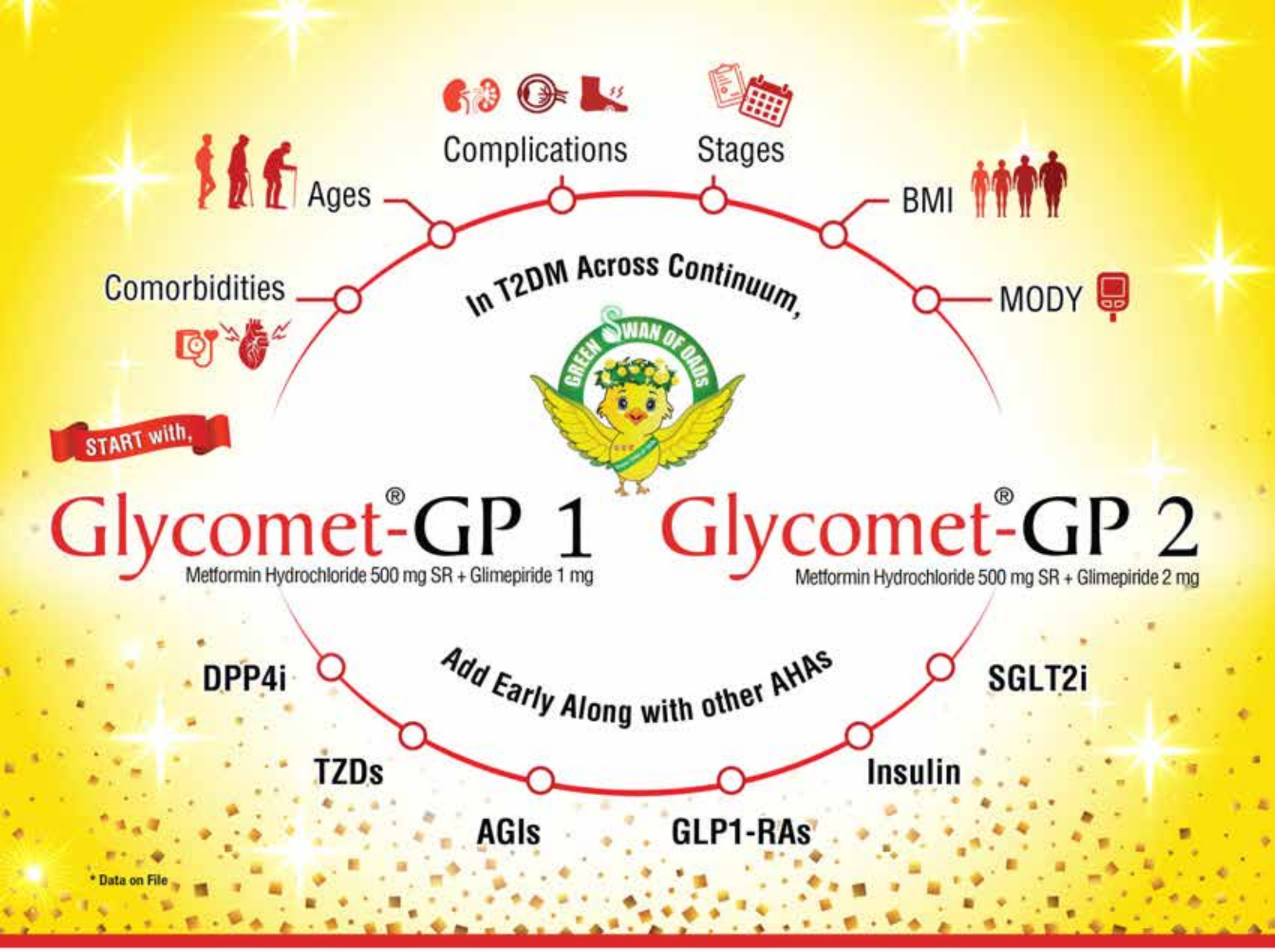


Beat Diabetes Win Life

NOTES

NOTES

NOTES



1. Asian Journal of Diabetology, Vol. 23, No. 2, April-June 2022: YALAMANCHI SADASIVA RAO etal, 2. Asian Journal of Diabetology, Vol. 23, No. 2, April-June 2022; SAUMITRA RAY etal, 3. Cureus 2020; 12(9): e10.7759/cureus.1070 4. CMARC Data 5. Healthplix Data 6. Lim L-L, Lau ESH, Cheung JTK, et al. Real-world usage of sulphonylureas in Asian patients with type 2 diabetes using the Joint Asia Diabetes Evaluation (JADE) register. Diabetes Obes Metab. 2022;1-14. Doi:10. 1111/dom.14865;

Prescribing Information

Information: Metformin hydrochloride (as prolonged release) and glimepiride tablets. Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/850/ Glycomet-GP 2/ Glycomet-GP 2/850/ Glycomet-GP 3/ Glycomet-GP 3/850/ Glycomet-GP 4/ Glycomet-GP 4/850/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte Abridged Prescribing Information **Composition:** Glycomet GP 0.5mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500mg and glimepiride IP 0.5mg.• Glycomet GP 0.5 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 0.5mg.• Glycomet GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. • Glycomet GP 1/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. • Glycomet GP 2: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 2 mg. • Glycomet GP 2/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 2 mg.• Glycomet GP 3: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 3 mg. • Glycomet GP 3/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 3 mg. • Glycomet GP 4: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 4 mg. • Glycomet GP 4/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 4 mg. • Glycomet GP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 1mg. • Glycomet GP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 2mg. • Glycomet GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 3mg. • Glycomet GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP mg. **Indication:** For the management of patients with type 2 diabetes mellitus when diet, exercise and single agent (glimepiride or metformin alone) do not result in adequate glycaemic control. **Dosage and Administration:** The recommended dose is one tablet daily during breakfast or the first main meal. Each tablet contains a fixed dose of glimepiride and Metformin Hydrochloride. The highest recommended dose per day should be 8 mg of glimepiride and 2000mg of metformin. Due to prolonged release formulation, the tablet must be swallowed whole and not crushed or chewed. **Adverse Reactions:** For Glimepiride: hypoglycaemia may occur, which may sometimes be prolonged. Occasionally, gastrointestinal (GI) symptoms such as nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhea may occur. Hepatitis, elevation of liver enzymes, cholestasis and jaundice may occur; allergic reactions or pseudo allergic reactions may occur occasionally. For Metformin: GI symptoms such as nausea, vomiting, diarrhea, abdominal pain, and loss of appetite are common during initiation of therapy and may resolve spontaneously in most cases. Metallic taste, mild erythema, decrease in Vit B12 absorption, very rarely lactic acidosis, Hemolytic anemia, Reduction of thyrotropin level in patients with hypothyroidism, Hypomagnesemia in the context of diarrhea, Encephalopathy, Photosensitivity, hepatobiliary disorders. **Warnings and Precautions:**: For Glimepiride: Patient should be advised to report promptly exceptional stress situations (e.g., trauma, surgery, febrile infections), blood glucose regulation may deteriorate, and a temporary change to insulin may be necessary to maintain good metabolic control. Metformin Hydrochloride may lead to Lactic acidosis; in such cases metformin should be temporarily discontinued and contact with a healthcare professional is recommended. Sulfonylureas have an increased risk of hypoglycaemia. Long-term treatment with metformin may lead to peripheral neuropathy because of decrease in vitamin B12 serum levels. Monitoring of the vitamin B12 level is recommended. Overweight patients should continue their energy-restricted diet, usual laboratory tests for diabetes monitoring should be performed regularly. **Contraindications:** Hypersensitivity to the active substance of glimepiride & Metformin or to any of the excipients listed. Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis, diabetic pre-coma). Severe renal failure (GFR≤30ml/min). In pregnant women. In lactating women.Acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents); acute or chronic disease which may cause tissue hypoxia (cardiac or respiratory failure, recent myocardial infarction, shock); hepatic insufficiency; acute alcohol intoxication; alcoholism. **Use in a special population:** Pregnant Women: Due to a lack of human data, drugs should not be used during pregnancy. Lactating Women: It should not be used during breastfeeding. Pediatric Patients: The safety and efficacy of drugs has not yet been established. Renal impairment: A GFR should be assessed before initiation of treatment with metformin containing products and at least annually thereafter. In patients at increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g. every 3-6 months.

Additional information is available on request.

Last updated: March 13, 2023

In case of any adverse events, kindly contact: pv@usv.in For the use of registered medical practitioner, hospital or laboratory.

USV Private Limited Corvette Team

Arvind Vithal Gandhi Chowk, B. S. D. Marg, Govandi, Mumbai - 400 088. | Tel.: 91-22-2556 4048 | Fax: 91-22-2558 4025 | www.usvindia.com

Scan the QR code to access full library of IDEJ -
https://usvmed.com/