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# Journal of Diabetes Education

To Dispel Darkness Of Diabetes

DIET MANAGEMENT

EXERCISE

MEDICATION

An Official Publication of
Association of Diabetes Educators
(India)

# Invokana®
## canagliflozin 100mg tablets

- Control diabetes with confidence[1]
- Significant **HbA1C** reduction[1]
- **KgA1C** resolution[1]

# MOTIVYST®
Canagliflozin 300mg

*DOES MORE... MUCH MORE*

## More to Deliver

- Only **dual SGLT1 & SGLT2** inhibitor in India[2,3]
- **2.56%** HbA1C and **5.2%** weight reduction[4,5]
- **35%** Increase in **GLP1 and PYY** levels[6,7]

# With CV and Renal Protection

HbA1C: Glycated Hemoglobin; CV: Cardiovascular; SGLT1: Sodium Glucose Linked Transporter 1; SGLT2: Sodium Glucose Linked Transporter 2; GLP1: Glucagon like peptide 1; PYY: Peptide YY

**References: 1.** Jakher M *et al.* Diabetes, metabolic syndrome and obesity:targets and therapy; **2.** Sokolov V *et al.* Dierentiating the SodiumGlucose Cotransporter 1 Inhibition Capacity of Canagliflozin vs. Dapagliflozin and Empagliflozin Using Quantitative Systems Pharmacology Modeling. CPT: pharmacometrics & systems pharmacology. 2020 Apr;9(4):222-9; **3.** Mohan V *et al.* Remogliflozin Etabonate in the Treatment of Type 2 Diabetes: Design, Development, and Place in Therapy. *Drug Design, Development and Therapy*. 2020;14:2487; **4.** Stenlöf K, *et al. Diabetes Obes Metab.* 2013;15(4):372–82; **5.** Lawrence A. Leiter *et al. Diabetes Care.* 2015;38:355–364; **6.** P. Song et al, *Expert Opinion On Therapeutic Targets*, Apr 2016; **7.** Polidori *et al. Diabetes Care.* Vol 36, Aug 2013.

**Abridged Prescribing Information**
For the use of a Registered Medical Practitioner or a Hospital or Laboratory
**Canagliflozin tablets 100 mg / 300mg**
**INVOKANA®**

**Composition and Strength:** Canagliflozin 100 mg / 300mg. Each 100 mg tablet contains 102 mg Canagliflozin hemihydrate, equivalent to 100 mg Canagliflozin. Each 300 mg tablet contains 306 mg Canagliflozin hemihydrate, equivalent to 300 mg of Canagliflozin. **Pharmaceutical form:** 100 mg - The tablet is yellow, capsule-shaped, immediate-release and film-coated, with "CFZ" on one side and "100" on the other side. 300 mg - The tablet is white, capsule-shaped, immediate-release and film- coated, with "CFZ" on one side and "300" on the other side. **Therapeutic Indications:** INVOKANA® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with Type-2 Diabetic Mellitus. INVOKANA® is indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease. INVOKANA® is indicated to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type2diabetes mellitus and diabetic nephropathy with albuminuria > 300 mg/day#. **Dosage and Administration:** The recommended starting dose for adult > 18 years is 100 mg or 300 mg once daily orally preferably before the first meal of the day. A starting dose of 100 mg once daily should be used in patients on loop diuretics and patients ≥ *75 years of age. (A) Dosage Recommendation for Glycemic Control and/or Reduction of a Major Adverse Cardiovascular Event (MACE) in Patients with CVD:* In patients with an eGFR 45 mL/min/1.73 m² to < 60 mL/min/1.73 m², the dose of INVOKANA® is limited to 100 mg once daily. The 300 mg dose may be considered for patients with an eGFR > 60 mL/min/1.73 m², who need tighter glycemic control and who have a low risk of adverse reactions associated with reduced intravascular volume with INVOKANA® treatment. *(B) Dosage Recommendation for Chronic Kidney Disease and Albuminuria (> 300 to ≤ 5000 mg/g):* In patients with an eGFR 30 mL/min/1.73 m² to < 90 mL/min/1.73 m², the dose of INVOKANA® is limited to 100 mg once daily. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Warnings and Precautions:** INVOKANA® has not been studied in pediatric patients (< 18 years), patients with type 1 diabetes and is therefore not recommended for use. INVOKANA® should not be used for the treatment of diabetic ketoacidosis or in patients with an eGFR< 45 mL/min/1.73 m² [CrCl < 45mL/min] for the purpose of glycemic lowering and/or Reduction of a Major Adverse Cardiovascular Event (MACE) in Patients with CVD. 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This serious rare infection, called necrotizing fasciitis of the perineum, is also referred to as Fournier's gangrene. **Drug Interactions:** The metabolism of INVOKANA® is primarily via glucuronide conjugation mediated by UDP glucuronosyl transferase 1A9 (UGT1A9) and 2B4. INVOKANA® neither inhibits cytochrome P450 CYP1A2, CYP2A6, CYP2C19, CYP2D6, or CYP2E1, CYP2B6, CYP2C8, CYP2C9, nor induces CYP1A2, CYP2C19, CYP2B6, CYP3A4 at higher than therapeutic concentrations. INVOKANA® is a P-glycoprotein (P-gp) substrate and inhibits P-glycoprotein mediated transport of digoxin with low potency. Please refer to full prescribing information for further details. **Pregnancy, Breast-feeding and Fertility:** There are no adequate and well controlled studies in pregnant women. INVOKANA® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known if INVOKANA® is excreted in human milk. A risk to the breast-fed child cannot be excluded. The effect of INVOKANA® on fertility in humans has not been studied. **Cardiovascular and renal outcomes:** INVOKANA® significantly reduced the risk of first occurrence of the primary composite endpoint of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke (HR: 0.86; 95% CI 0.75,0.97). Each MACE component contributed to the overall composite. Subjects treated with INVOKANA® had a lower risk of hospitalization for heart failure compared to those treated with placebo. In the CANVAS Program, for time to first adjudicated nephropathy event (doubling of serum creatinine, need for renal replacement therapy, and renal death), the HR was 0.53 (95% CI:0.33, 0.84) for canagliflozin (0.15 events per 100 patient-years) versus placebo (0.28 events per 100 patient-years). **Adverse reactions:** In clinical studies of INVOKANA® the most commonly reported adverse reactions during treatment (≥ 5%) were vulvovaginal candidiasis, urinary tract infection, and polyuria or pollakiuria. Other adverse reactions in clinical studies of INVOKANA® that occurred at a rate < 2% in placebo-controlled studies were adverse reactions related to reduced intravascular volume (postural dizziness, orthostatic hypotension, hypotension, dehydration, and syncope), skin rash, and urticaria. In the clinical development program, events of DKA were reported in 0.2% of patients treated with INVOKANA®. In long-term clinical studies of INVOKANA® in type 2 diabetes patients with established cardiovascular disease (CVD) or at least two risk factors for CVD, an approximately 2-fold increased risk of lower limb amputation (primarily of the toe and midfoot) has been observed in patients treated with INVOKANA®. **Overdose:** In the event of an overdose, it is reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment as dictated by the patient's clinical status. Canagliflozin was negligibly removed during a 4-hour hemodialysis session. Canagliflozin is not expected to be dialyzable by peritoneal dialysis. **Storage:** Do not store above 30OC. Keep out of sight and reach of children.
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**For complete prescribing information, please contact:**
**Johnson & Johnson Private Limited.**
Arena Space, Behind Majas Depot, Off J.V. Link Road, Jogeshwari (E), Mumbai 400060

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MOTIVYST® 100 mg significantly reduced the risk of the primary composite endpoint based on a time-to-event analysis [HR: 0.70; 95% CI: 0.59, 0.82; p<0.0001] MOTIVYST® 100 mg also significantly reduced the risk of hospitalization for heart failure [HR: 0.61; 95% CI: 0.47 to 0.80; p<0.001]. **Adverse reactions:** In clinical studies of MOTIVYST® the most commonly reported adverse reactions during treatment (≥ 5%) were vulvovaginal candidiasis, urinary tract infection, and polyuria or pollakiuria. Other adverse reactions in clinical studies of MOTIVYST® that occurred at a rate < 2% in placebo-controlled studies were adverse reactions related to reduced intravascular volume (postural dizziness, orthostatic hypotension, hypotension, dehydration, and syncope), skin rash, and urticaria. In the clinical development program, events of DKA, were reported in 0.2% of patients treated with MOTIVYST®. 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PHARMACEUTICAL COMPANIES OF Johnson & Johnson

# JOURNAL OF DIABETES EDUCATION

To Dispel Darkness of Diabetes

**Vol. 10** **Number 1** **January-March, 2022**



## CONTENTS

# Story of Insulin: Hundred - Year Saga

**Hemraj B. Chandalia***

## Introduction:

Discovery of Insulin and its clinical use started in 1921-1922, hence we are familiar with this molecule for a century. It was the first remedy used in diabetes and continues to hold the most pre-eminent position amongst the medications used in diabetes. The 100-year saga of insulin includes the rigor of science which was continuously applied to the study of this molecule, its amino acid sequence, its tertiary structure, its measurement in health and disease, its synthesis and further designing its analogues. This molecule continues to attract the attention of scientists and path-breaking research on this molecule may give us tools to make the life of a diabetic more comfortable.

## Discovery of Insulin:

The facts surrounding the discovery of insulin are fascinating and have been the subjects of many books, including a very interesting one written by Bliss Federick Banting, an orthopedic surgeon who approached Prof McLeod at the University of Toronto asking for access to his laboratory in the summer of 1920. With some trepidation, McLeod allowed him access and made a medical student, Charles Best to join him as an assistant. He allowed a meagre budget to buy a small number of dogs for the proposed experiments. The duo toiled hard till Banting suddenly came upon an idea described earlier by other scientists. He thought of ligating the pancreatic duct of the dogs to cause atrophy of the exocrine pancreas, leaving the islets intact. Thereafter, the pancreas could be used to make a crude extract to be injected in other pancreatectomized dog with severe hyperglycemia and ketosis. This procedure led to a remarkable improvement in the pancreatectomized dog. The original idea was possible because of the previous description of Islets of pancreas, appropriately named by Opie as Islets of Langerhans. Similar work was in progress in the laboratory of Pulesco, a Polish investigator, but Banting and Best were the front-runners in this race and are credited for the discovery of insulin. John Collip, a biochemist at the university was involved in purifying the insulin to some extent leading to reduced incidence of unpleasant reactions. The patent for insulin isolation was awarded to the University of Toronto for one dollar. Eli Lilly, the pharmaceutical company was given rights to manufacture insulin and later two other prominent companies Novo-Nordisk (initially two separate companies) in Europe and Sanofi in USA joined this journey.

## Purification of insulin:

The first insulin injection was given on January 11, 2022 to a Type 1 diabetic named Leonard Thompson. This resulted into a severe reaction, local and systemic. After a process of purification, the same patient received another injection of insulin on January 23, 2022, without any untoward reaction. The process of purification continued, thus resulting into purer and safer insulin. The insulin available till 1970's was derived from beef or pork pancreata, in some countries separately and in India as a veritable mixture of beef and pork insulin. It contained about 8% extraneous protein, causing frequent skin reactions like locally allergy, lipoatrophy and lipohypertrophy (Fig 1). Occasionally, it produced an anaphylactic reaction.

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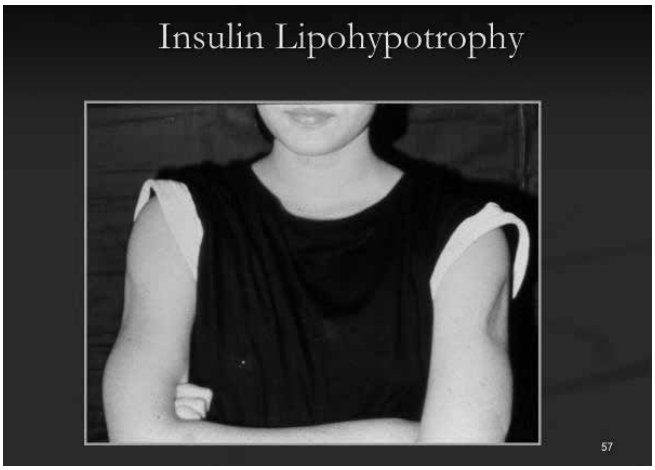
**Figure 1:**
Lipoatrophy produced by conventional insulin




Over the next two decades, from mid-50's to mid-70's, significant advances were made in the purification process as a result of which Novo Nordisk marketed monocomponent porcine insulin. Its use was attended by very rare skin reactions like allergic rashes and lipoatrophy. It is important to note that lipohypertrophy continues to occur even with human insulins derived from recombinant-DNA technology and even with use of insulin analogs because of the fact that proliferation of adipose tissue is a basic physiological action of insulin and repeated injections at the same site promotes lipohypertrophy.

**Prolongation of Insulin action:**

As early as in 1925, with large-scale use of insulin it was realised that regular insulin had a short duration of action and multiple doses were required in children to maintain fair glycemic control. Hence, efforts were mounted in producing insulins with prolonged action. In 1936, Scott and Fisher used protamine, a protein derived from fish, to meet this objective. In 1948, Hagedorn succeeded in introducing Neutral Protamine Hagedorn (NPH) insulin, which continues to be in used at present. It continues to be the most inexpensive basal insulin, but has serious limitations. In 1951, Halls Møller described Lente insulin, which is made by adding zinc chloride. This results in a mixture of 30% fast acting and 70% extended action insulin. Presently, these are discontinued primarily because the mixture of regular and lente or NPH insulin can alter the ratio of regular and extended action insulin, especially if not injected soon after mixing. The search for long acting insulin was again intensified in the mid-80's when the concept of a basal-bolus insulin therapy was developed. The structure of these insulins is unlike that of human insulin and hence they are considered as insulin analogs.

**Contribution of Basic Sciences in Insulin Development:**

From mid-50's to the early part of 20$^{th}$ century, a series of path-breaking scientific discoveries revolutionalised the area of newer insulin development (Table 1 and Table 2). The most basic was determining the amino-acid sequence of the insulin molecule, done by Fredrick Sanger. At that time, it was the first and the only protein which had been sequenced. This established the fact that all proteins have a fixed amino acid sequence. Sanger was awarded the Nobel Prize in Chemistry for this work in 1958. Interestingly, Sanger was awarded a second Nobel Prize in Chemistry in 1977 for describing a method for determining the nucleotide sequence of a protein. This method is called Sanger Sequencing method or Chain-Terminating Method. Thereafter, Dorothy Hodgkin used the X-ray crystallography technique to establish the three-dimensional structure of insulin. This was important, as it showed the folding of the molecule which determines the reactivity of the amino acids. For this work, she was awarded the Nobel Prize in Chemistry in 1969. The next important discovery was made by Rosalyn Yalow and Soloman Berson, when they described the radioimmunoassay of insulin levels in the body fluids. Thus, insulin was the first protein whose microgram concentration in the blood was measured. This gave a great impetus to the study of insulin levels in health and disease. Yalow was awarded the Nobel Prize in medicine in the year 1977. Soon it was realized that

young diabetics had near-total insulinopenia while most adult diabetics showed plethora of insulin in their circulation. This was forerunner of the concept of insulin resistance, proposed by Reaven. In 1967, Donald Steiner of the University of Chicago discovered that human insulin was produced as a single amino-acid chain, which was termed pro-insulin. It consisted of A and B chains, with a connecting peptide, labelled C-chain. This discovery was useful subsequently to scientists attempting to manufacture human insulin by genetic engineering.

**Table 1:**

**Chronology of Discovery of Insulin and Advances in Insulin Science**

| |
|---|
| 1869: Islet tissue of pancreas described by Paul Langerhans, a German physician. Later on, these islets were named by Opie as Islets of Langerhans. |
| 1908-1921: Georg Ludwig Zuelzer (1909), Earnest Lyman Scott (1912), John Murlin (1913), Israel Kleiner (1919), Nicolas Paulesco (1921) worked along the same line as Banting. |
| 1921: Banting conceived the idea of ligating the pancreatic duct, let exocrine tissue atrophy, extracting pancreas and injecting in pancreatectomised dogs. |
| 1921-23: Isolation of Insulin by Banting and Best, Purification of insulin by John Collip, Beginning of large scale production. |
| 1950: Prolongation of Insulin action; NPH (1950) by Hagedorn, and Lente (1952) by Hallas Møller<br>Monocomponemt (Purified insulin) |
| 1980: Recombinant DNA technology used to produce human insulin |
| 1996: First Insulin analogue, Lyspro insulin produced by Eli Lilly company |
| 2000: Insulin glargine introduced |
| 2004: Detemir insulin introduced |
| 2015-2017: Glargine 300, Degludec and insulin Degludec-Aspart (Coformulation) introduced |

**Table 2:**

**Nobel Prizes for Advancing Insulin Science**

| Year | Scientist | For |
|---|---|---|
| 1923 | Banting and Macleod in Medicine (Banting shared with Best and MacLoed with Collip) | Discovery of insulin |
| 1958 | Fredrick Sanger in Chemistry | Determining amino-acid sequence of Insulin |
| 1964 | Dorothy Hodgkin for Chemistry | For determining 3-D structure of Insulin |
| 1977 | Rosalyn Yalow for Medicine | For developing the Radio immunoassay of Insulin |
| 1980 | Walter Gilbert for Chemistry | For developing the method of DNA sequencing |

The seeds of genetic engineering techniques were sown with the landmark work of Maxam and Walter Gilbert. These scientists described the method of nucleotide sequencing, thus elucidating the structure of a DNA. For their work, Walter Gilbert received the Nobel Prize in chemistry in 1980. Soon this knowledge was used to insert the insulin sequence in the plasmids of E.coli and transfer the same to the bacilli which then produces insulin. This insulin could be harvested from multiplying bacteria. Eli Lilly successfully marketed Human insulin (brand name: Humilin) in 1982 by using this technology. Later on other companies produced human insulin by using alternative vectors like an yeast.

**Insulin Analogues:**

When animal insulin was in use, it was observed that des-alaninated porcine insulin retained its activity when alanine at B-30 position in B-chain was removed. Thereafter intensive laboratory modifications of insulin were made by a number of amino acid deletion and substitution processes. Structure of IgF1 showed that Lysine at 28 position and Proline at 29 position conferred the property of allowing it to exist in monomeric

form. Interchanging of Proline at B28 and Lysine at B29 in human insulin produced the first insulin analogue by Eli Lilly, called Lyspro (Humalog). This change reduced the tendency of insulin molecules to self-associate with each other and produce hexamers. The conversion of these hexamers to dimers was required before absorption, thus delaying the action of human insulin. Thus lyspro insulin was made as the first rapid-acting analogue. By using various strategies (Table 3), a variety of analogs were created. Presently, three rapid acting insulin analogues are in clinical use: Lyspro, Aspart and Glulisine. Their effect peaks in 15-30 minutes after injection and dissipates in about 2-3 hours as compared to that of Human regular insulin which has a peak effect at 1-2 hours and dissipates at 4-5 hours after injection. Thus, the rapid acting analogues offer a more physiological action profile. The fast Aspart is another innovation, made by adding L-arginine and niacinamide to Aspart, which accelerates initial absorption. This doubles the insulin available in the initial half-hour after injection and increases the initial glucose-lowering effect two-fold as compared to Aspart. Between the three rapid acting analogues (Lyspro, Glulisine, Aspart) the first half-hour post-injection insulin available in descending order are: glulisine, aspart and lyspro, but these differences have not been shown to be clinically significant.

**Table 3:**

**INSULIN ANALOG DESIGN**

| Strategy | Example |
|---|---|
| Charge repulsion | B9, Asp (Ser), B12 Glu (Val), B28 Asp (Pro) |
| Steric hindrance | B 12 IIe (Val) |
| Hydrophilic into hydrophobic interfaces | B16 Glu (Tyr), B 17, Gln (Leu) |
| Removal of Cation metal-binding sites | B10 Asp (His), Thr (His) |
| Mimicking IGF-1 structure | B 28 Lys (Pro), B 29 Pro (Lys) |
| residues in native human insulin are shown in parentheses | |

Studies on physiological insulin secretion in healthy subjects have shown spurts of non-meal related insulin secretion in the basal state which produces a steady level of serum insulin throughout the day and night. This prompted the search for a good basal insulin analogue, which can mimic the physiological basal insulin secretory profile. Earlier on, NPH insulin in two doses was used to provide the basal effect. However, each dose peaked its effect after 4-5 hours, and increased the likelihood of hypoglycemia, mainly in concert with human regular insulin often used in combination. Thus, search was on for peakless insulin. This was partly fulfilled by Detemir insulin and further improved by successive basal insulin's like Glargine U100, Degludec and Glargine U300. A good insulin analog, both rapid or fast-acting or long acting must fulfill a set of important criteria (Table 4). In case of rapid-acting insulin, the peak should be in 30 minutes and the effect should abate in about 2 hours. In case of basal insulin, there should be a steady level for 24-30 hours, without any peak. We have almost reached near-ideal insulin but the intra-subject variability of insulin response, measured as coefficient of variation continues to make the insulin response unpredictable. The coefficient of variation is almost 40% with earlier basal insulins like NPH and Detemir, but has reduced to 15-20 % with Degludec and Glargine 300. This variability may be dependent upon the physical state of insulin molecules like formation of hexamers, zinc concentration and variable injection site. However, a part of it is probably related to the fact that biological responses can vary day to day even with the similar exposure to insulin and are extremely complex to analyse and predict. The coefficients of variation of insulin response has been less with short and rapid acting (Human regular, Lyspro, Aspart and Glulisine) insulin and is in the range of 10-20%. The long-acting analogues like Degludec and Glargine 300 have produced a predictable response with less overall and nocturnal hypoglycemia. Co-formulated insulin like Ideg-Aspart is a combination of 70% Degludec and 30% Aspart insulin. It is superior

to insulin mixtures, because both components of insulin in the co-formulation maintain their original pharmacokinetics with great consistency.

**Table 4:**

**PROFILE OF AN IDEAL INSULIN ANALOG**

| Must resemble Human Insulin in: |
|---|
| 1. Hypoglycemic effect |
| 2. Counter-regulation |
| 3. Antigenicity |
| 4. Insulin receptor binding & dissociation in vitro & in vivo |
| 5. IgF-1 receptor binding & dissociation in vitro and in vivo |
| 6. Lack of teratogenicity |
| 7. Low intraindividual coefficient of variation (? 10%) |

**Insulin Delivery:**

Insulin injections were made by using reusable glass syringes along with 21 gauze, half inch-long needles. This obviously caused pain while injecting. Over the decades, improved and modern syringes and needles are of the disposable type and needles are 31 gauze and 4 mm long. These are virtually painless. Further improvements came with the introduction of insulin-pens in mid-1980's. They offer the ease of administration in accurate doses. Most important improvement occurred with the introduction of insulin pumps. The early prototype pump of a fairly large size was described in 1969 but wearable, small size pumps were made in the 1990's. These pumps became smaller and sturdier over the years. The pumps are primarily indicated for Type 1 diabetics, who are difficult to control without hypoglycemia even with the use of Multiple Dose Insulin (MPI) therapy. The pumps have capacity to deliver insulin in a near-physiological manner. The coefficient of variation of insulin response is reduced to 2 %, hypoglycemia and a flexible life style is possible when on the insulin pump. The insulin dosages need to be calculated by the patient, based on frequent blood sugar tests. These are called open-loop systems. This loop is being closed now by synchronizing a blood glucose sensor, to the pump software and pump injector in an automatic process. Minimed 670 G is one such insulin pump. The glucose sensors used in these systems or for diabetics in general also are very important in giving an impetus to this method of insulin delivery. These sensors have enabled the user to gain a detailed insight into their food, exercise and insulin interaction.

**Future Insulin Therapy:**

Insulin science is steadily progressing to provide a better form of insulin preparation. Several important areas of investigations are fascinating. Smart insulin may possess the attributes of entering the blood stream as per the physiological need, based on the ambient blood glucose. A hepato-selective insulin was being considered by some investigators. As is well known, about half of the injected insulin is utilized in the liver in the first sojourn through the liver. The hepato-selective insulin even if injected systemically will mimic this natural partitioning of insulin and could be an important advance. Analogs will be further developed to give ideal insulins, hopefully affordable and available in all parts of the world.

**Summary:**

The discovery of insulin and its journey over the past hundred years is an interesting story of human trial and tribulations and the victory of science. The story is not yet complete, even after the award of five Nobel prizes for the research related to the Insulin Science. This story includes the scenes of human endeavors, exemplary collaboration and fierce competition. It will continue to inspire scientists and clinicians for a long time to come.

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# HELICOBACTER PYLORI

**Jayshri Jain***

## Introduction:

***Helicobacter pylori*** (*H. pylori*) is a spiral-shaped bacterium that lives in the stomach lining. It causes 90 percent of ulcers, which are sores in the stomach or the duodenum. Prior to 1982, when this bacterium was discovered, doctors thought that lifestyle, spicy food, acid, stress caused most ulcers. Now doctors know that most ulcers are caused by an *H. pylori* infection, which can mostly be cured with the appropriate antibiotics. Australian scientists, Barry J. Marshall and J. Robin Warren first discovered *Helicobacter pylori* for which they won the Nobel Prize in 2005 for Physiology and Medicine.

Infection with *Helicobacter pylori* is common. About two-thirds of the world's population suffers from this infection. The *H. pylori* bacteria stick to the layer of mucus in the digestive tract and cause inflammation which can cause this protective lining to break down. This breakdown is a problem because the stomach contains strong acid intended to digest food. Without the mucus layer to protect it, the acid can eat into stomach tissue which leads to ulcers. These may then bleed, cause infections or keep food from moving through the digestive tract.

## How *Helicobacter pylori* enters and make us sick:

*H. pylori* enters the body through food, water or utensils. It is more common in countries or communities that lack clean water, have poor hygiene standards and sewage systems. One can also pick up the bacteria through contact with saliva or other body fluids of infected people.

## Symptoms:

Ulcers can cause a variety of symptoms or no symptoms at all, with the most common ulcer symptoms including:

- Pain or discomfort especially in the upper abdomen part
- Bloating
- Feeling full after eating a small amount of food
- Lack of appetite
- Nausea or vomiting
- Dark or tar-colored stools
- Ulcers that bleed can cause a low blood count

Less commonly, chronic gastritis causes abnormal changes in the stomach lining, which can lead to certain cancers. However, it is uncommon to develop cancer as a result of *H. pylori* infection. Nevertheless, as *H. pylori* infection is widespread it is considered to be an important cause of stomach cancer. People who live in countries where *H. pylori* infection occurs at an early age are at greater risk of stomach cancer.

## Diagnosis:

If one does not have symptoms of an ulcer, the doctor probably will not advice the *H. pylori* test. But, if one has symptoms or has had in the past, it is best to get tested. As medicines like non-steroidal anti-inflammatory drugs (NSAIDs) may damage the stomach lining, it is very important to get the right treatment.

To diagnose *H. pylori,* there are several ways out of which the most commonly used tests are the following:

- **Breath tests** — Breath tests also known as urea breath tests require that one drink a specialized solution containing a substance that is broken down by the *H. pylori* bacterium. The breakdown products can be detected in the individual's breath.

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- **Stool tests** — Stool tests are the test that detect the presence of *H. pylori* protein in stool.
- **Blood tests** — Blood tests can detect specific antibodies (proteins) that the body's immune system develops in response to the *H. pylori* bacterium. However, this is limited in use because of low accuracy.
- **Upper gastrointestinal endoscopy**: ***In a hospital*** setting, the doctor will use a tube with a small camera, called an endoscope, to look down the throat and into the stomach and the upper part of the small intestine. The procedure may also be used to collect a sample that is examined for the presence of the bacteria. One may be asleep or awake during the procedure, and be given medications to make one comfortable.
- **Upper GI tests:** In a hospital setting, one is asked to drink a barium paste and the doctor studies the stomach lining on X-ray. The fluid coats the throat and stomach and the ulcers stand out clearly on the image.

**Treatment for *Helicobacter pylori:***

If one has ulcers caused by *H. pylori,* one will need treatment to kill the germs, heal stomach lining, and keep sores from returning. It usually takes one to two weeks of treatment to show improvement.

The doctor prescribes a variety of drugs for this malady. The options include:

- Antibiotics: Amoxicillin, Clarithromycin, Metronidazole, Tetracycline or Tinidazole. Patient will most likely need two from this group.
- Most of the treatment regimens include a proton-pump inhibitor which decreases the stomach acid production, thus allowing tissues damaged by the infection to heal. Examples of proton- pump inhibitors include Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole, Dexlansoprazole and Esomeprazole.
- Bismuth subsalicylate, which also kills *H. pylori* along with antibiotics.
- Medicines are given which block the chemical histamine which prompts the stomach to make more acid. These are Cimetidine, Famotidine and Pepcid.

The treatment could mean one has to take a large number of pills per day for a few weeks. But it is very important to adhere to it. If not taken, bacteria in the body can become resistant which makes infection harder to treat. If the medication does not agree with one, the doctor needs to be informed. After two weeks of treatment, the doctor may order the breath or stool test to make sure the infection is gone.

**Prevention:**

Following steps help to prevent the *H. Pylori* infection:

- Always wash hands after usage of bathroom and before preparing or eating food. Teach everyone to do the same in family.
- Avoid usage of unclean water. If salad, ensure it is cleaned well.
- Eat food which is thoroughly cooked.
- Though stress and spicy foods do not cause ulcers, but it delays the healing process. Talk to the health care advisor about stress management, diet and smoking habits.

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# SHORT CHAIN FATTY ACIDS

**Rima Ved***

## Introduction:

Short chain fatty acids (SCFA) are produced by microbial fermentation or breakdown of non-digestible carbohydrates which escape digestion and absorption in the small intestine. The main end products of fermentation include Acetate, Butyrate, Propionate and Lactate. Table 1 describes food sources and potential benefits of different fibre types.

**Table 1:**

**Naturally occurring fibre types:**

| Fibre Type | Food Sources | Potential Benefits |
|---|---|---|
| Soluble highly fermentable oligosaccharides | Legumes, Pulses, Nuts and Seeds<br>Wheat, Rye<br>Onions, Garlic and Artichoke | Rapidly fermented in proximal colon and terminal ileum to produce SCFA |
| Soluble highly fermentable fibre | Legumes and Pulses<br>Barley<br>Raw Bananas<br>Buckwheat, Millet, Oats<br>Cooked and Cooled-Pasta,<br>Potato, Rice | Rapidly fermented in proximal colon to produce SCFA (mostly butyrate) |
| Intermediate soluble fermentable fibre | Psyllium Husk and Oats | SCFA: moderately fermented in the colon to produce SCFA. |
| Insoluble slowly fermentable fibre | Some Vegetables and Fruit<br>Wheat Bran<br>Wholegrain Cereals<br>Rye<br>Brown Rice, Wholemeal Pasta, Quinoa<br>Flax Seed | These fibres are slowly fermented to produce SCFA along the length of the colon. |
| Insoluble, non-fermentable Fibre | High Fibre Grains and Cereals, Nuts and Seeds<br>Skin Of Fruit and Vegetables | Poorly fermented, hence less production of SCFA. |

*Source: Eswaran et al, 2013*

## Mechanism of SCFA Production and Action in the Gut:

Figure 1 describes the mechanism of synthesis of SCFA mainly Acetate, Propionate and Butyrate.

Acetate: One of the major SCFA, it is produced by the gut bacteria by two mechanisms: through Acetyl Co-A or the Wood-Ljungdahl pathway.

Propionate: In the succinate pathway, this is produced from phosphoenolpyruvate (PEP) and is also produced by the Acrylate pathway where lactate is reduced to form propionate.

Butyrate: Two acetyl Co-A molecules combine leading to the production of Butyrate.

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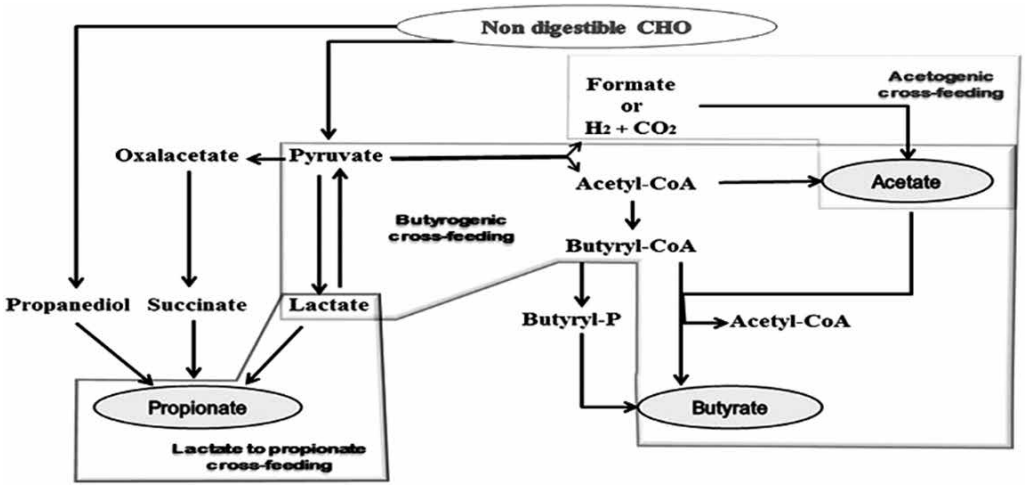
**Figure 1:**

**Known Pathways for Biosynthesis of SCFAs from Carbohydrate Fermentation and Bacterial Cross-Feeding**




*Source: Koh A et al, 2016*

**Short chain fatty acids (SCFA) and Metabolic Health:**

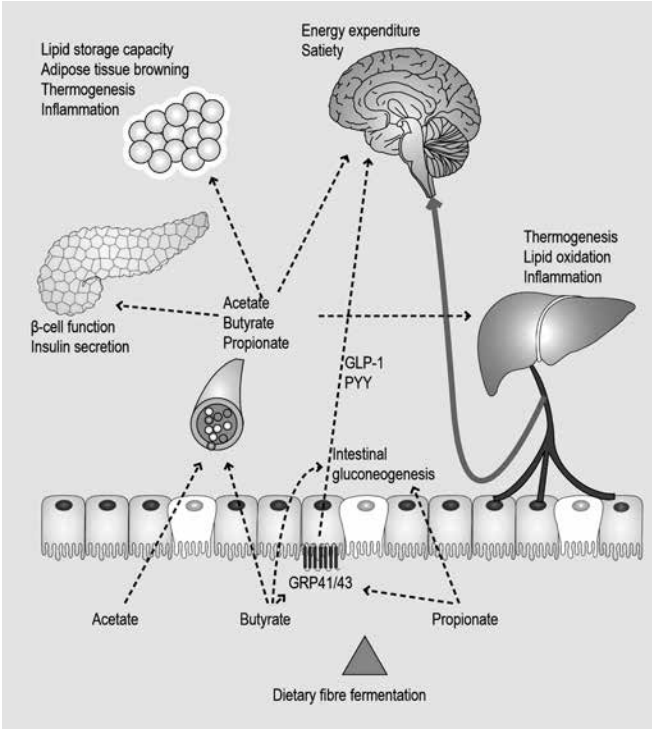
As seen in figure 2, SCFA enhances the release of Glucagon-like peptide 1 (GLP-1) an incretin which is secreted from intestinal cells. GLP-1 in turn binds to a receptor on the pancreatic β cells and stimulates secretion of insulin. Hence assisting in glucose metabolism. SCFA, along with GLP-1 further stimulate secretion of Gastric Inhibitory Polypeptide (GIP) and Peptide YY (PYY) in adipocytes which reduces fat accumulation. Glucose homeostasis (the balance between Insulin and Glucagon to maintain blood glucose) is affected by SCFAs such as Propionate and Butyrate. They bind to GPR41 and GPR43 - protein-coupled receptors (GPCR's) expressed in the adipose tissue, gut, and the peripheral nervous system, thereby affecting satiety and glucose homeostasis. The glucose, when released sends out neural signals to the brain, inducing satiety and insulin sensitivity. Insulin sensitivity refers to the responsiveness of the cell towards insulin. Increased insulin sensitivity indicates that blood glucose is being used more effectively by the cells. This in turn causes a decrease in the blood glucose level.

**SCFA, Fibre and Diabetes:**

Acetate decreases appetite by signalling the brain inducing satiety and thus assisting in the mitigation of Type 2 diabetes mellitus. It also improves glucose tolerance and reduces appetite by modifying the expression of the appetite regulatory neuropeptides in the hypothalamus. A

**Figure 2:**

**Short Chain Fatty Acids (SCFA) and Metabolic Health**




*Source: Blaak et al, 2020*

cross- sectional study conducted among a cohort of male and female adult relatives of people with Type 2 diabetes, with measurement of 3-day food records revealed that intake of both soluble as well as insoluble dietary fibre is inversely associated with insulin resistance thus enhancing insulin sensitivity.

In dietary supplementation studies, plasma propionate was seen to cause reduction in post-meal insulin levels, help glucose homeostasis, improve gut function and reduce inflammation. This resulted in increased insulin sensitivity. When propionate was taken with inulin, it showed an improved insulin resistance. Inulins belong to a class of dietary fibre known as fructans and is a type of prebiotic. It's not digested or absorbed in the stomach. It stays in the bowel and helps certain beneficial bacteria to grow. Inulin, is a starchy substance found in a wide variety of fruits, vegetables, and herbs including wheat, onions, bananas, leeks, artichoke and asparagus. Another study conducted by Beth N. Hopping et al pointed out that fermentation of insoluble fibre led to SCFA production and thereby an improvement in insulin sensitivity. Propionate supplementation in healthy women for seven weeks, reduced fasting sugar levels and increased the release of insulin, which helped establish a link between SCFA and glucose homeostasis and preventing the progression of Type 2 diabetes. A further analysis of 17 overweight/ obese subjects over a period of 72 hours showed that, consumption of insoluble fibre improved insulin sensitivity, thus reducing risk of Type 2 diabetes.

**Concentrations of SCFAs as a function of diet:**

A study conducted by Archana Singh et al, gave a recommended allowance of dietary fibre as 35-40 g/day for an adult to be taken in small amounts, but at regular intervals. In another study, insulin sensitivity was assessed by Gower et al, where in healthy sedentary women for a four week period a snack such as maize (resistant starch) of 15-30g per day or waxy corn containing rapidly digestible starch was given. The higher dose of resistant starch significantly improved insulin sensitivity in the insulin-resistant group but it did not affect those parameters in women classified as insulin sensitive during baseline assessments.

SCFA production in healthy adults consuming test meals containing 20–25 g/day of either soluble corn fibre or resistant starch (high-amylose maize) for one week was examined in another study. Although, the soluble corn fibre treatment enhanced total SCFA production, the resistant starch treatment resulted in a greater proportion of colonic-derived butyrate.

Since SCFA production is difficult to measure in vivo, most experiments have been done in-vitro with intestinal or faecal microbiota as inoculum. The type and amount of fibre consumed affects composition of the intestinal microbiota and consequently the type and amount of SCFAs produced. In Western societies, the average human diet contains approximately 20–25 g fibre per day. In diets, that are high in fruit and vegetables, the fibre content may reach up to 60 g per day. Fermentation of the carbohydrates reaching the cecum amounts to a production of 0.24–0.38 kg of SCFAs for body weight which is equivalent to 10% caloric requirement in humans. In humans, the effect of dietary fibre intake has been studied mainly by measuring the SCFA concentrations in faeces followed by calculating the total rate of SCFA excretion. In most studies, acetate is the predominant SCFA in the faeces, followed by propionate and butyrate.

**Effect of thermal processing on composition of Gut Microbiota:**

The main objective of the study conducted by Sergio Perez-Burillo et al was to shed light on changes in gut microbiota produced after fermentation of meat, fruits, vegetables, cereals, and legumes while paying special attention to the influence of cooking techniques and heat damage. In order to achieve this goal, chicken, banana, red pepper, bread, and chickpeas were selected as food products and were exposed to the most common culinary techniques for each of them (frying, boiling, grilling, roasting, toasting vs raw). Following this, microbial changes were

linked to the type of food, culinary treatment or heat intensity (thermal damage monitored through furosine and HMF-furfural content). All samples were subjected to an in-vitro digestion process followed by an in-vitro fermentation to mimic physiological processes in the human gut. SCFA such as acetic acid, butyric acid and propionic acids were assessed in this study.

**Acetic acid:** Bread produced the highest amount (74.8 μmol/g), whereas chicken produced the lowest one (5.9 μmol/g).

**Propionic acid**: Chickpeas were the highest producers (52.1 μmol/g), whereas chicken showed the lowest value (12.2 μmol/g).

**Butyric acid**: The levels of butyric acid ranged from 51.5 to 9.3 μmol/g for red pepper and bread, respectively.

Overall, banana produced the highest amounts of SCFAs followed by chickpeas, whereas chicken yielded the lowest amounts. Secondly, the possible influence of the culinary treatment over SCFAs production was studied and results are shown below.

**Boiled and grilled chickpeas:** There was no statistically significant difference in acetic acid or propionic acid production. However, butyric acid production was significantly higher in grilled chickpeas. One possible explanation could be the formation of melanoidins, which can behave as a fibre in the gut, therefore increasing butyric acid production.

**Bread:** In the case of bread, there were no significant difference between raw or toasted bread regarding acetic and propionic acid production. However, butyric acid production was, significantly higher in raw bread.

**Red pepper**: Red pepper showed significantly higher production of acetic acid when roasted and butyric acid after frying. However, no significant difference was observed in propionic acid production. In this sense, products that appear as a consequence of the thermal treatment, such as melanoidins, could be responsible for the different SCFA production.

**Banana:** No difference was found between acetic acid production for roasting or frying, but both had a significantly higher production than raw banana. Propionic acid production was also significantly higher in roasted banana, though there were no differences among raw or fried fruit. Both roasted and fried banana yielded significantly higher amounts of butyric acid than raw banana, while the fried fruit had significantly higher values than the roasted one. In this case, it also seems that the culinary treatment has some effect on SCFA production and that, as in the case of chickpeas and red pepper, cooking favoured SCFA production.

**Chicken:** Roasted, fried, and grilled chicken showed a significantly higher production of acetic and butyric acid than boiled chicken. However, no difference was found in the case of propionic acid.

**Conclusion**: SCFAs have a role to play in increasing insulin sensitivity, increasing uptake of insulin by cells, signalling brain inducing satiety and thus assist in reducing blood sugar levels. High-amylose-maize-resistant-starch modified with acetate and butyrate (HAMSAB)

When administered for six weeks with a follow-up at twelve weeks in adults with long standing Type 1 diabetes, an increased stool concentrations of acetate, propionate and butyrate was found. This resulted in an increased shift in the composition and function of the gut microbiota correlating with lower HbA1c and basal insulin requirements. Since SCFAs are a result of fermentation in colon, it reduces pH of colon. The lower pH limits the growth of some harmful bacteria like *Clostridium difficile*. In general, fruits, vegetables, beans and whole grains like wheat, oats and barley are all good sources of prebiotic fibres and need to be included on a daily basis to ensure optimum glycemic control.

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# QUESTION AND ANSWERS

**Q. Where is the best place to draw blood from for measuring blood glucose levels?**

**Ans.** Blood glucose level can be measured by two methods. One is by pinprick in the fingertip using a glucometer and another is by withdrawing blood from a vein and getting it checked in a laboratory. The former method can be carried out at home. In this, one has to prick the finger with a needle and a single, small drop of blood is enough to measure blood glucose. Most of the laboratories withdraw blood sample from the vein at the elbow and check blood glucose. There may be 10% difference between the two (finger prick method gives lower figure as some tissue fluid may mix with the blood).

**Q. How by testing urine can we monitor diabetes patients?**

**Ans.** Our body has a unique organ called the kidney. Whenever sugar is in excess in our blood this organ excretes it out in the urine. Kidney works as a safety-valve for our body. Sugar only appears in the urine when its level in the blood increases to 180 mg% or more. This is because kidney cannot tolerate sugar beyond 180 mg% and starts excreting it out in the urine. This is the threshold level and it is at this point that urine gives a positive test for sugar.

People with diabetes may get their urine checked but it will only test positive if its level in the blood is 180 mg% or more. Thus this test is not always a true indicator of one's disease status. However, if one wants to get one's urine checked for diabetes very frequently, there are paper sticks called urine testing strip available in the market for this purpose. These sticks should be dipped in the urine and if they show a colour change it means sugar is present.

**Q. What is diabetic coma?**

**Ans.** Diabetic coma is loss of consciousness occurring as a result of very high blood sugar. Its causes are similar in both Type 1 and Type 2 diabetes, but with the important difference that other abnormalities of the blood chemistry may contribute to coma in Type 1 diabetes. These other abnormalities occur as a result of the near total lack of insulin present in Type 1 diabetes. For this reason, while blood sugar is almost always very high in people with Type 2 diabetes who are in diabetic coma, being several hundreds to 2000 mg/dl or more, it can be less elevated in people with Type 1 diabetes and as low as only 200 or 300. In the case of Type 1 diabetes, diabetic coma can occur solely as a result of having insufficient insulin in the body (e.g. running out of or not taking one's insulin), while in the case of Type 2 diabetes, there is almost always another stress to the body that precipitates a coma, such as infection or dehydration. If the serious abnormalities of blood chemistry that lead to a diabetic coma are not corrected rapidly, death can occur. Although the derangements in blood chemistry are more complex and severe in Type 1 diabetes than in Type 2 diabetes, there is a higher mortality in a Type 2 diabetic coma because people suffering from it tend to be older, in less robust health and with more cardiac risk factors. Also, symptoms of nausea, vomiting, and abdominal pain occur in Type 1 diabetes leading to coma and the diagnosis may be made earlier as a result. In the early stages of coma in Type 2 diabetes, abnormalities of brain function and consciousness are more prominent due to the extreme degree of dehydration. Moreover, the illness that precipitated the coma may carry its own serious health risks. Although only a minority of patients with diabetes will succumb to coma, it remains an important medical emergency that requires immediate intervention.

**Q. I hear a lot about footwear and foot care for diabetes. Why is this so important?**

**Ans.** Proper care and protection of the feet are extremely important for people with diabetes. This is due to the fact that the feet are frequently affected by nerve damage in diabetes, with a resultant loss of protective sensation. Protective sensation is the perception of potential injury,

such as awareness of sharp, rough, or excessively hot or cold objects or friction, such as rubbing against the inside of shoes. When this is impaired, it is possible for the person with diabetes to sustain wounds, abrasions, burns, or freezing of which he or she may be unaware. Other type of injuries such as bites and blisters can similarly occur unnoticed. Even fractures of the bones of the foot can occur painlessly when more severe forms of diabetic nerve damage are present. The most serious consequence of unperceived injury is infection. Because the blood supply to the feet may also be impaired, the healing and immune response to both the injury and the infection can be compromised, so that a chronically infected wound results. The most dangerous consequences of chronically infected wounds are spread of infection to the deeper tissues, including the bones, and entry of infectious organisms into the bloodstream, which can lead to blood poisoning (septicemia) or spread by the bloodstream to other body tissues. Both of these consequences can cause severe illness or even death. Local infection of the bones of the feet can require amputation, since infection in the bone (called "osteomyelitis") is very difficult to treat. Even powerful modern antibiotics given intravenously over several weeks may fail to completely eradicate infection in bone when its blood supply is poor. Diabetic nerve damage in the feet may lead to disturbance of the mechanics of the foot, such that pressure may occur on bony areas not designed to bear that. This can cause unusual prominences of the bones of the feet on all of their surfaces, which are more prone to injury. Corns, calluses, cracks, fissures, and ulcers of the feet can all occur in people with diabetes in the absence of specific injury, but as a result of abnormal pressure distribution caused by nerve damage. Hence, it is very important to protect the feet by wearing suitable footwear, not going barefoot, paying attention to the environment (i.e. removal or covering of protruding furniture legs etc. and hard, abrasive floor surfaces), performing daily inspection of the feet, foot hygiene, nail care and prompt cleaning and dressing of minor injuries.

**JJ**

# RECIPES

## VEGETABLE OATS PANCAKE

**Ingredients**

| | |
|---|---|
| Rolled oats blended into coarse (flour in a mixture) | 100 gm |
| Grated carrots | 50 gm |
| Spinach (palak), finely chopped | 50 gm |
| Coriander (dhania), finely chopped | 30 gm |
| Oil for greasing and cooking pancakes | 2 tsp |

**Procedure:**

1. To make vegetable oats pancake, combine all the ingredients including the oats flour, carrots, spinach, coriander, green chillies, spices (optional or can add any spice of your choice), and salt according to taste. Add 1 cup of water to all the ingredients in a deep bowl. Mix well to form a batter of dropping consistency (not too watery or too solid)
2. Heat a non-stick tava (griddle) and grease the griddle with ¼ tsp of cooking oil
3. Pour a spoonful of the batter on it and spread in a circular motion to make round circle shaped pancakes
4. Cook, using ¼ tsp of cooking oil, till it turns light brown in colour from both sides
5. Repeat the same procedure for the remaining batter to make 3 more pancakes
6. Serve the hot piping vegetable oats pancakes with chilled curd/yogurt and green coriander chutney

**Provides 4 servings**

**Nutritional information per serving:**

| Energy (kcal) | Carbohydrate (gm) | Protein (gm) | Fat (gm) | Fiber (gm) | Glycemic Index |
|---|---|---|---|---|---|
| 488 | 64 | 14 | 17 | 5 | Medium |

**Special features:**

- A healthy recipe for breakfast.
- A high fiber recipe.

# QUINOA VEGETABLE UPMA

**Ingredients:**

| | |
|---|---|
| Quinoa, washed and drained | 50 gm |
| Cooking oil | 2 tsp |
| Mustard seeds | ¼ tsp |
| Asafoetida | ¼ tsp |
| Finely chopped green chillies | ½ tsp |
| Finely chopped ginger | ¼ tsp |
| Curry leaves | 2 pcs |
| Finely chopped onions | ¼ cup |
| Green peas | ¼ cup |
| Finely chopped carrots | ¼ cup |
| Red chilli powder | ¼ tsp |
| Finely chopped coriander | ¼ tsp |
| Lemon juice | ½ tsp |
| Salt to taste | |

**Procedure:**

1. First step to making quinoa vegetable upma, is to wash the quinoa grain well and soak it for a period of 1 hour. After 1 hour, drain excess water using a strainer. Keep the washed quinoa aside.
2. Heat the oil in a deep non-stick pan, add mustard seeds and asafoetida and saute on a medium flame for a few seconds.
3. Add the green chillies, ginger and curry leaves and saute on medium flame for a few seconds.
4. Add the onions and saute on a medium flame for 2 minutes
5. Then add the quinoa and saute on a medium flame for 1 minute
6. put chilli powder, salt and 2 ½ cups of hot water and mix well. Cover with a lid and cook on a medium flame for 20 to 22 minutes, while stirring occasionally.
7. Switch off the flame and garnish with coriander and lemon juice.
8. Serve the quinoa vegetable upma immediately with a cup of hot tea.
4. Serve hot with chilled curd

**Provides 2 servings**

**Nutritional information per serving:**

| Energy (kcal) | Carbohydrates (gm) | Protein (gm) | Fat (gm) | Fiber (gm) | Glycemic Index |
|---|---|---|---|---|---|
| 223 | 20 | 6 | 12 | 7 | Medium |

**Special features:**

- A healthy recipe for breakfast.
- A high fiber recipe.

**JJ**

# HOW'S KNOWLEDGEABLE ARE YOU ?

1. Which of the following are not auto-antibodies is a marker for Type 1 diabetes?
   A. Antibodies to GAD65
   B. Antibodies to tyrosine phosphatase IA-2 and IA-2 beta
   C. Zinc transporter 8 (ZnT8)
   D. None of the above

2. Which of the following are the pharmacological effects of Metformin?
   A. Reduced glucose absorption from the gut
   B. Facilitation of glucose entry into muscle
   C. Inhibition of gluconeogenesis in the liver
   D. All of the above

3. Sulphonylureas increase insulin secretion by Beta cells. Sulphonylureas act by binding to the sulphonylurea receptor and inhibit:
   A. ATP dependent K+ channel
   B. Voltage-gated calcium channel
   C. GLUT-2
   D. None of the above

4. Which of the following enzyme would be more active in diabetic patients?
   A. Glucokinase
   B. Fatty acid synthase
   C. Lipoprotein lipase
   D. Hormone-sensitive lipase

5. The therapeutic goal of managing and preventing hyperlipidemic complications of diabetes mellitus include:
   A. LDL <100 mg/dL
   B. HDL> 40 mg/dL
   C. Triglycerides <150 mg/dL
   D. All of the above

6. All of the following drugs are oral hypoglycemic drugs except
   A. Metformin
   B. Sulphonylureas
   C. Thiazolidinediones
   D. Insulin

7. Which is of the following is not the consequence of insulin deficiency in carbohydrate metabolism?
   A. Increased blood glucose concentration
   B. Increased glycogen breakdown
   C. Decreased peripheral glucose utilization
   D. Decreased gluconeogenesis

8. Which of the following is the consequence of insulin deficiency in protein metabolism?
   A. Decreased protein breakdown
   B. Increased synthesis of amino acids
   C. Decreased ureagenesis
   D. Increased protein synthesis

9. Which of the following is not the consequence of insulin deficiency in lipid metabolism?
   A. Increased triglyceride breakdown
   B. Increased level of free fatty acids
   C. Increased ketogenesis
   D. Increased lipogenesis

10. What is the first step in the management of diabetic ketoacidosis?
    A. To provide fluids intravenously
    B. To provide insulin
    C. To initiate insulin and fluids simultaneously
    D. To provide bicarbonate

**ANSWERS:**

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

# MYTHS AND FACTS

1. **Myth: Insulin means one has failed to manage diabetes efficiently.**

   Fact: Needing insulin does not mean that you have failed to manage your diabetes well. Because Type 2 diabetes is a progressive disease, eventually your pancreas is just not able to keep up with your body's need for insulin, no matter what efforts have been done to manage your diabetes. When other medicines no longer keep your blood glucose on target, insulin is often the next logical step for treating Type 2 diabetes.

2. **Myth: Insulin does not work.**

   Fact: Although many people think of diabetes as a "sugar" problem, actually diabetes is an insulin problem. The insulin's used today are very similar to the insulin that the body naturally makes indigenously. In fact, insulin is the best and most effective way to lower your blood glucose.

3. **Myth: Insulin injections are painful.**

   Fact: Although no one likes injection shots, most people are surprised to experience how little an insulin injection hurts. Insulin does not "sting" going in, and the needles are very small, fine and thin. Most people find that it is less painful than a finger- stick test done to monitor blood glucose levels. In fact, insulin injection administered to infants in their sleep, is so painless that the infant does not realise it all and continues to sleep.

4. **Myth: Insulin causes hypoglycemia.**

   Fact: It is true that insulin can cause a low blood glucose response. However, with the newer or long-acting insulins, hypoglycemia is less likely to occur. It is rare for people with Type 2 diabetes to pass out from low blood glucose. You can learn how to prevent, recognize and treat hypoglycemia and thus avoid severe reponses.

5. **Myth: Insulin is habit forming.**

   Fact: You cannot get addicted to insulin. Insulin is a natural substance the body requires. If one is concerned that people may see one taking an insulin shot in a public place and think that they are using illegal drugs, ask the health care provider and opt for insulin pen would work instead.

6. **Myth: Insulin is too expensive.**

   Fact: Treatment of diabetes is expensive, no question about it. Generally, however, insulin is usually less expensive than using several different types of oral medications. As prices vary a great deal at different stores, inquire for the best prices on insulin and other supplies both offline and online or directly with the insulin manufacturing company representative.

7. **Myth: Insulin means that my life will change.**

   Fact: Many people believe that once they start insulin, they can no longer be independent, live alone, travel or eat out. None of this is true. With planning, one can continue as earlier. Ask the health care provider to refer one to a diabetes educator who can help plan the insulin regime coordination with the lifestyle.

   Actually, many people find that their lives do change with insulin – but for the better. They have more energy, more flexibility in their schedule, and feel positive about themselves. After initiating insulin, people wonder why they waited so long.

**JJ**

# CERTIFIED DIABETES EDUCATOR COURSE

***Dr Chandalia's DENMARC in association with Help Defeat Diabetes Trust (HDDT) presents to you a course to be a Certified Diabetes Educator (CDE)!***

Help Defeat Diabetes Trust (HDDT) is a registered, non-profit public trust, having amongst its many objectives, the main objective of promoting education and awareness about diabetes among people from different fields.

**Who can enroll?**

Graduates in Nutrition, Nursing, Pharmacy, Occupational and Physiotherapy.

**What is the duration of the course?**

6 months, including 3 months (300 Hours) of hands-on training and experience with a recognized mentor in your own town (see this on our website).

**How can I do this course from my place of residence?**

The Mentor can be selected from the particular locality and under whom the training can be done.

**How will I get the course material?**

All course material is available online on our website.

**What are the course fees?**

The standard fees for the course are INR 10,000/- only.

**Where can I get more information about this course?**

Kindly visit our website **http://www.helpdefeatdiabetes.org** or you can get in touch with us on our email ID heldefeatdiabetesinfo@gmail.com.

Help Defeat Diabetes Trust
• Education • Patient Care • Research

# CERTIFIED DIABETES EDUCATOR COURSE

# HELP DEFEAT DIABETES TRUST Announces

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**Duration:** 6 months

**Course Highlights:**

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Criteria for award:

- To complete the course in given time frame i.e. 6 months.
- To secure highest marks in the current year.

For further details visit helpdefeatdiabetes.org

# MEMBERSHIP FORM

## Association of Diabetes Educators (ADE)

(For eligibility criteria: Check Website www.diabeteseducatorsindia.com)

Name ……..……..

Address ……..……..

……

Telephone: Res: ….....…… Office: ……..... Cell: ……

E-mail id: ….....……..

Educational Qualifications:.....……..……

……

……

Work Experience: ….....……..……

……

……

Currently employed at: .....……..……

……

Certificates attached*: .....……..……

……

Please pay the membership fees through NEFT / RTGS to the following bank account.

The details are as folllows:

Account name: Association of Diabetes Educators

Account type: Savings Account

Name of the bank: Bank of India

Account number: 006610110001734

IFSC Code: BKID0000066

……..……

Signature

# CHALLENGES IN DIABETES EDUCATION

## AN AWARD FOR PROBLEM RESOLUTION IN DIABETES EDUCATION

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**Prize money of Rs. 10,000 for reporting a problem case**

Dr. Chandalia's HDDT aims to enhance the quality of Diabetes education in India by creating a world-class research and education environment and to build up a platform of networking and knowledge sharing within diabetologists and/or diabetes educators.

Challenges in Diabetes Education 2021 places special emphasis on supporting educational initiatives that have the potential to improve and significantly revolutionize diabetes care, enhance self-management and/or support patients with Type 1 or Type 2 Diabetes Mellitus. The educator should describe an individual or group case history and identify the problem in diabetes education. Furthermore, s/he should describe the plan of education to resolve the issue, partly or totally. The issue described may be related to patient perceptions, knowledge, behaviors and implementation of advice given. S/He should describe her struggle in resolving the issue including her triumphs and failures, the methodologies used and ethical, socio-economic and behavioral aspects of the case.

General Rules and Regulations regarding the eligibility Criteria for the Award

- The applicant of the Award should be a citizen of India and member of Association of Diabetes Educators.
- The case discussion should be on the subject of Diabetes Education.

The best case chosen by a group of referees will be awarded "Challenges in Diabetes Education Award- 2021" - which will carry a cash prize of Rs 10,000. The awardee will get the opportunity to present the case in the annual meeting of Association of Diabetes Educators and publish it in the journal of Diabetes Education.

**The last date for the submission is 30th December, 2021 !!!!**

(Instructions for authors is available on website www.diabeteseducatorsindia.com)

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**Abbreviations:** HbA1c: Glycated Hemoglobin, PK/PD: Pharmacokinetic/Pharmacodynamic

**References:** 1. Bolli GB et al. Diabetes Obes and Metab 2015;17(4):386–394. 2. Rosenstock J, et al. Diabetes Care 2018;41:2147–54. 3. Toujeo® Prescribing Information. Dated: June 2017 Source: CCDS Version 1.1 dated June 2016. 4. Riddle M et al. Diabetes Technol Ther. 2016;18:252–7. 5. Bailey TS,et al. Diabetes Metab 2018;44:15–21. 6. Ghosh R, Nair A, Shah N et al. Toustar: the first reusable pen for insulin glargine 300 U/mL with dedicated replaceable cartridge to be launched in India. Poster P239 ATTD Conference June 2021

For full prescribing information of Toujeo please visit-
https://www.sanofi.in/-/media/Project/One-Sanofi-Web/Websites/Asia-Pacific/Sanofi-IN/Home/science-and-innovation/for-healthcare-professionals/product-information/Toujeo_201706.pdf?la=en

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***OAD:** Oral Antidiabetic Drugs

**Reference:** Standl E, et al. Diabetes Care. 2016; 39(Suppl 2): S172-S179.

For further details kindly contact : Sanofi India Limited ,Sanofi House, CTS No. 117-B, L&T Business Park, Saki-Vihar Road, Powai, Mumbai - 400072, India.

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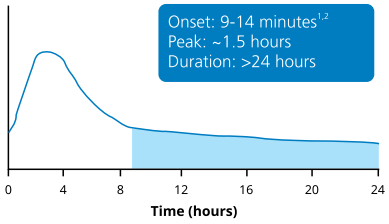


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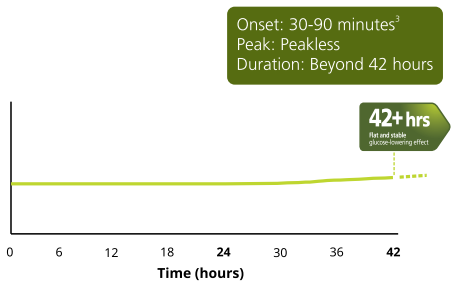


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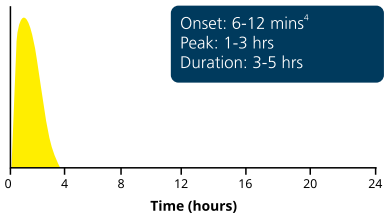


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**References: 1.** Haahr H *et al. Clin Pharmacokinet* (2017) 56:339–354. **2.** Ryzodeg™ CDSCO approved package insert version (8-9564-26-010-7), dated (11 JAN 2019). **3.** Mannucci E *et al. Drug Healthc Patient Saf.* 2015 Jul 10;7:113-20. **4.** Danne T *et al. Pediatr Diabetes.* 2018 Oct;19 Suppl 27:115-135.