

NEXT STEP LIVING LONGER BOOKS

LIVING LONGER BOOKS Finally A Revolution in Indian Health Care

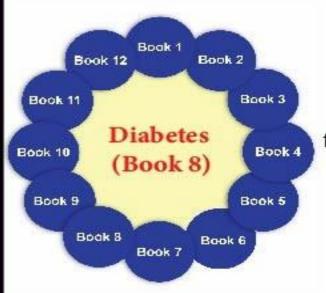
Diabetes - Book 8

SELECTIVE SODIUM-GLUCOSE

TRANSPORTER-2 (SGLT2) INHIBITORS

IN 2021: No reason for kidneys to fail!!

Before 1921: Yes, You would have died. (year of Nobel Prize for Insulin)



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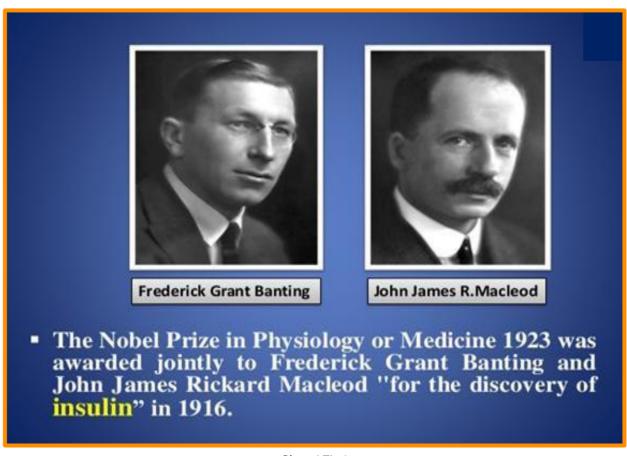
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Introduction



Chap1Fig1

<u>Insulin was discovered in 1921 leading to a nobel prize. In 2021 we have 12 groups of medicines for medicine diabetes.</u>

Think About It!

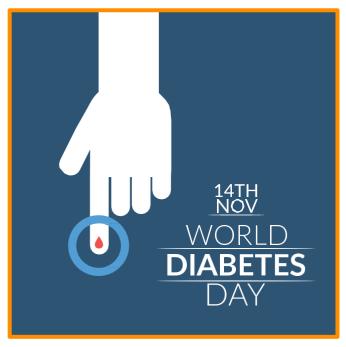
Before 1921

Every child who was born with Type 1 diabetes or lack of insulin would eventually die.

The discovery of insulin or should we say the discovery of insulin as a medicine has changed the history of diabetes and its treatment.

In 2021

We can now have a healthy life with functioning kidneys till very end!!

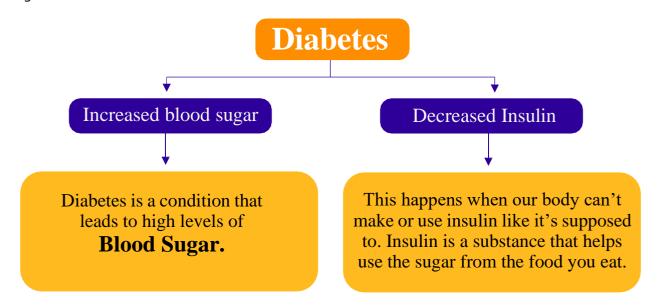


But yes, we have 12 to 13 different groups of medicines for high blood sugar.

<u>The golden principle</u> of the medicinal treatment of diabetes is that we start with one medication early in the course of treatment of diabetes.

We keep adding medicines as needed to control our blood sugar (along with diet & exercise)

Chap1Fig1



The Golden Principle in Management of high blood sugar (Diabetes)

The golden principle of the medical treatment of diabetes is that Once we have high blood sugar (Diabetes) – exercise and diet management are needed life-long.

Together diet, exercise and medications – all will help!!

Risk of taking medications are minimal as compared to the benefits that we receive from these medicines!

1. We start with **one medication** early in the course of treatment of diabetes

Start with one medication

2. <u>Targets</u> for blood sugar control is decided by physician.

Decide Targets

3. Usual target is $\underline{\mathbf{HbA1c}} < \underline{\mathbf{7}}$

HbA1c < 7

4. As youngish we are more, we want to keep blood sugar is close to 100mg

Blood sugar close to 100mg

Continued

The golden principle of the medical treatment of diabetes is that Once we have high blood sugar (Diabetes) – exercise and diet management are needed life-long.

- **5.** <u>Today in 2021</u> are several groups of excellent medicines are available:
- a) which can <u>bring down our blood sugar</u> by different mechanisms of action.
- **b)** As a golden rule, what we should start with <u>one medicine</u> if our blood sugar is not extremely high.
- c) And as time goes on.

 We can add a second medicine.

Start with one medicine, if blood sugar is not very high

Start with one medicine, Add a second medicine, if needed And add a third medicine, if necessary

d) Or we can even add a third medicine which works by a different mechanism.

Diet and exercise are an integral part of high blood sugar management!

Diet and exercise are an integral part of high blood sugar management!

Purpose of medical management and medici nes for diabetes is:

• To manage our blood sugar



Chap3Fig1

• As close to 100mg as possible



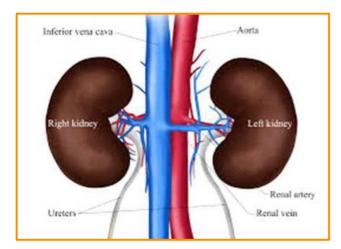
Chap3Fig2

• And HbA1c < 7



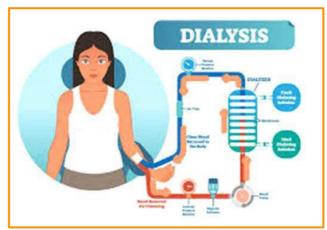
Chap3Fig3

• To prevent kidney failure



Chap3Fig4

And no dialysis



Chap3Fig5

• No heart attack (Diabetes is literally one of the reasons)



Chap3Fig7

• No blindness (Diabetes is one of the reasons)



Chap3Fig8

• No amputation of leg (Diabetes is one of the reasons)

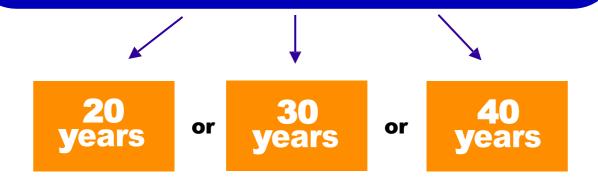


Chap3Fig9

Yes, Diabetes management can really reduce complications

If we manage diabetes from day one or **even before we have actual diabetes** (called prediabetes),

Complication are dramatically delayed by



Is it true?

√ Really Yes! it is True

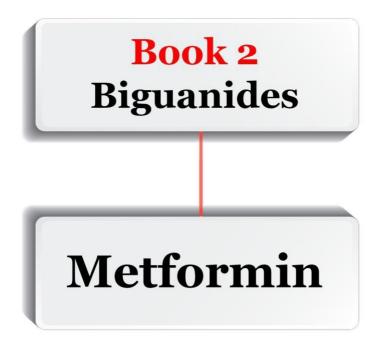
Today in 2020/2021 we have excellent medicines available

There are a number of medicines available in the market today for the treatment of Diabetes.

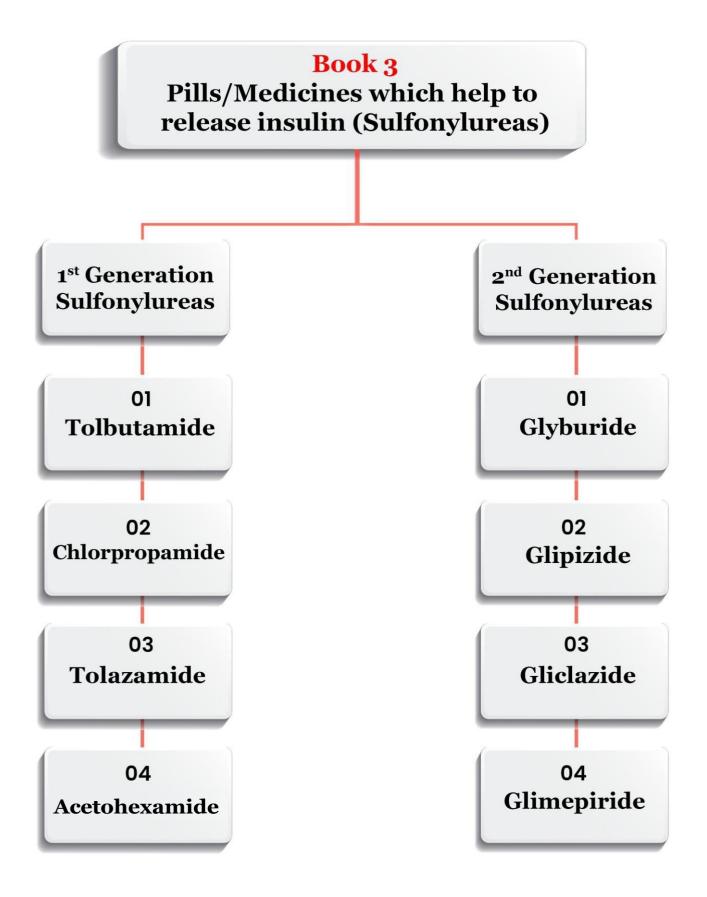
The main groups which these medicines belong to are:

Book-2 Biguanides

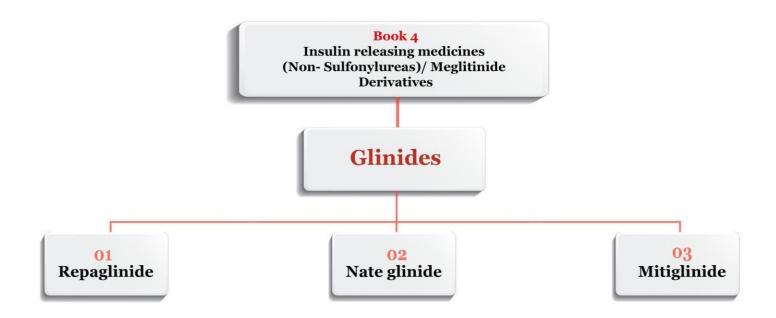
Metformin: The most famous and most used medicine and 1st medicine to start the treatment of diabetes.



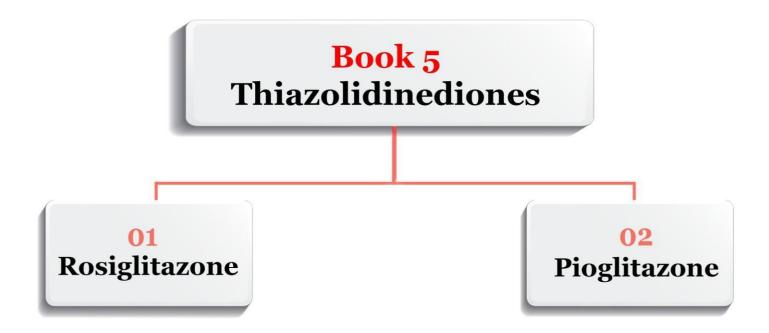
Book-3 Pills/Medicines which help to insulin (Sulfonylureas)



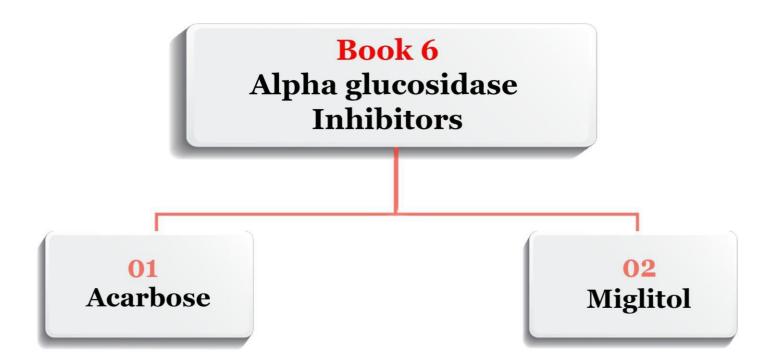
Book-4 Insulin releasing medicines (Non- Sulfonylureas)



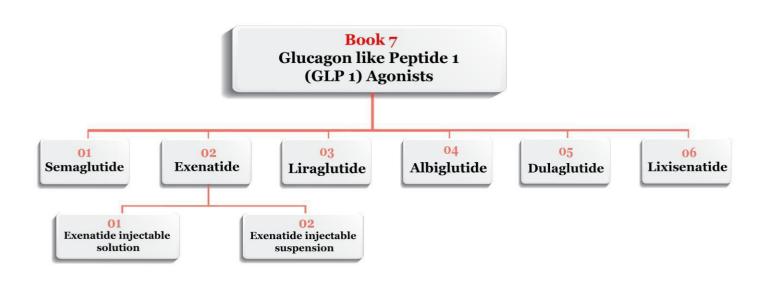
Book-5 Thiazolidinediones



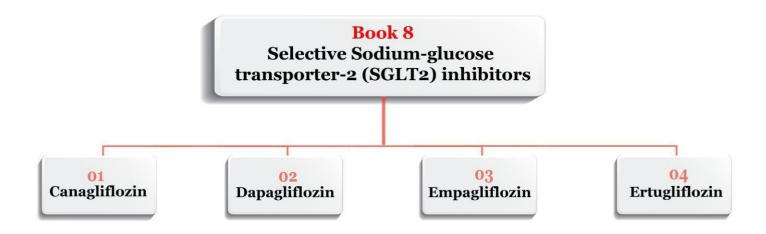
Book-6 Alpha glucosidase Inhibitors



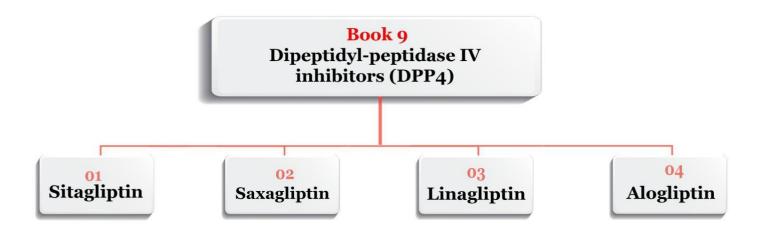
Book-7 Glucagon like Peptide 1 (GLP 1) Agnostics



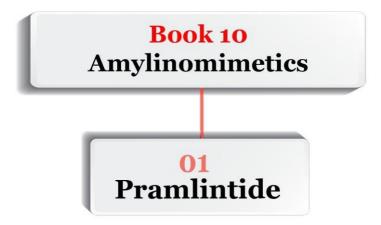
Book-8 Selective Sodium-glucose transporter-2 (SGLT2) inhibitors



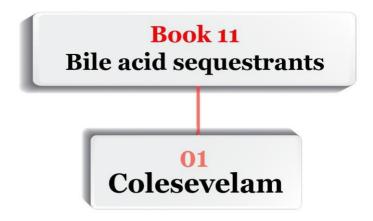
Book-9 Dipeptidyl-peptidase IV inhibitors (DPP4)



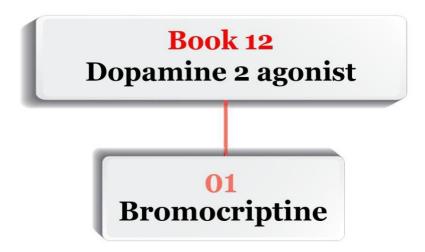
Book-10 Amylinomimetic group



Book-11 Bile acid sequestrants



Book-12 Dopamine 2 agonist



There are dramatic advances in treatment of diabetes today in 2021

Think About It!

We are **NOT** perfect; we don't need to be. But we **CANNOT** quit trying either.

Every high sugar management prescription always includes:

- 1. Medicine(s),
- 2.Diet, and
- 3. Exercise

Without these, it is impossible to achieve our targets.





or

By Injection below our skin (very easy to learn)



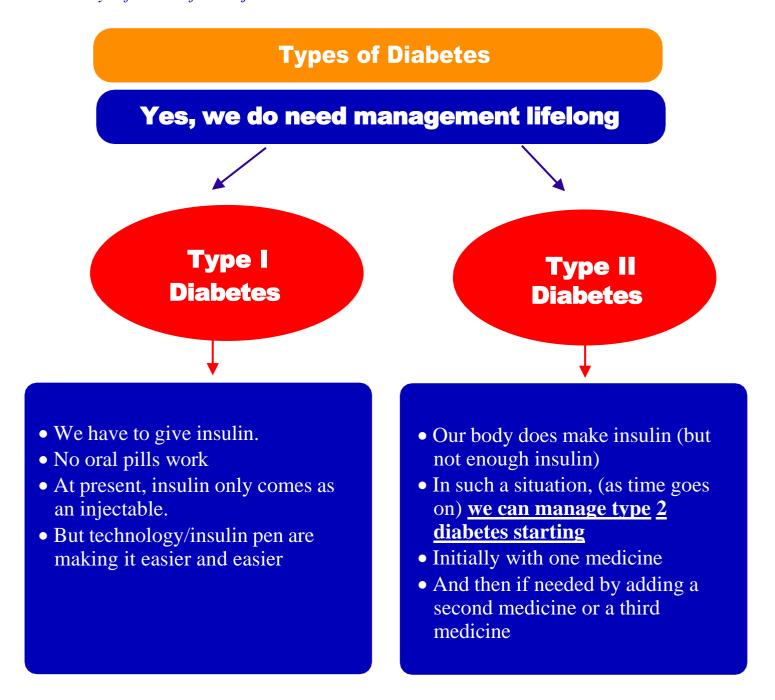


Chap6Fig2

Type 1 vs Type 2 Diabetes

Think About It!

We were always scared of needles and injection needs some degree of training so that it does not lead to any infection on the injected place. We have to follow the sterile techniques that do not lead to any infection of the injection sites.



How do we decide less dose or more dose of medicines

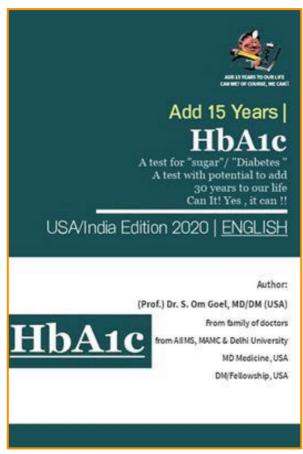
Think About It!

Our blood sugar changes all day based on

- Our meals,
- Level of activity etc.
- HbA1c remains stable over three months.

How do we decide less dose or more dose or combination of medicines?

I. We actually use HbA1c as our guideline for the treatment of diabetes.



Chap8Fig1

II. We set up a <u>target for HbA1c</u> in diabetic managementand we want that the <u>HbA1c</u> always remains 7 or less than 7.

HbA1c < 7

III. <u>If we met our target</u>, we can lower the dose.

Start with one medicine, if blood sugar is not very high

IV. If our HbA1c is high, then we can give the increased dose or add a 2nd pill or add even a 3rd pill.

Start with one medicine, Add a second medicine, if needed And add a third medicine, if necessary

Early diagnosis and early treatment: an absolute necessity in 2021

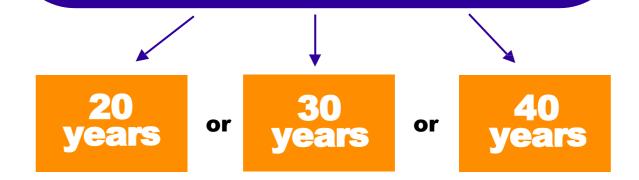
Think About It!

Every mom knows how her baby will start walking around in 1 year of age.

Every physician knows how to diagnose diabetes (called Prediabetes) year before you have any "symptoms".

Actually, if we can diagnose Diabetes, even before it happens to us (called as Prediabetes), we can really delay complications as mentioned and it will be a very wise thing to do.

Most important thing we have to understand is that if medicines are taken early in the diagnosis of high blood sugar/diabetes then it can delay complications related to diabetes by





Diabetes - Book 8 **SELECTIVE SODIUM-GLUCOSE** TRANSPORTER-2 (SGLT2) INHIBITORS

IN 2021: No reason for kidneys to fail!!

Before 1921: Yes, You would have died. (year of Nobel Prize for Insulin)

Farxiga – A New Medicine to Improve Blood Sugar Control

Think About It!

To be honest, when I was going through my nephrology/kidney/blood pressure training back in 90s, our professor and head of the nephrology/kidney department was doing a research on the new medicine.

In real life whenever we eat food, our blood sugar goes up. When all the sugar goes through the kidneys (it is filtered); but the kidneys absorb all the sugar back. This happens in a normal and healthy situation.

If slowly our blood sugar goes up to more than 180 which takes several years, then in that situation any blood sugar which is filtered and above 180 mg cannot be absorbed by the kidneys and shows in our urine.

Back in 70s and 80s that is how we diagnose sugar by urine test -- showing sugar in the urine.

But that also meant that you always have a type 2 diabetes for several years, minimum 5 to 8 years.

Our professor was doing a research on a medicine which will block or make kidney not to absorb any sugar or any filtered sugar so that all the sugar that is filtered we lose through our kidneys.

Think About It (cont'd)!

If our blood sugar is high, then most of the filtered blood sugar goes out in the urine as medicines block the absorption of the glucose by the kidneys.

In other words, they help us to bring our blood sugar down.

Since we also lose sugar which is a source of energy and which can be converted into the fat, we actually lose weight also.

So that was back in 90s and now this medicine finally came out and approved in 2014. So, think about it, it took almost 20 years to develop this medication.

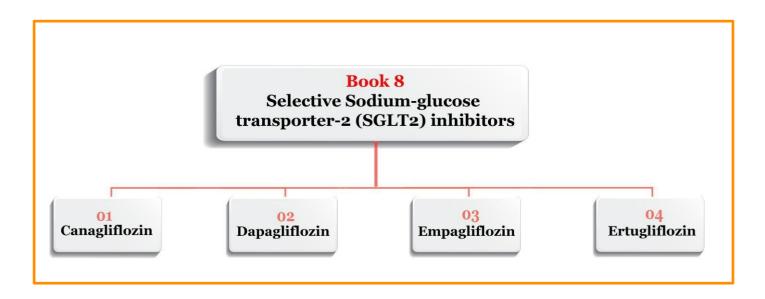
Those days, I thought a lot about it how it is going to work, is it really possible?

But till tells us, yes, it is possible, and it is an excellent medicine very popular now more in US and India by name of "Farxiga".

And it is used both for diabetes and weight loss.

Selective Sodium-Glucose Transporter-2 (SGLT2) Inhibitors

Selective Sodium-Glucose Transporter-2 (SGLT2) Inhibitors



These medicines have same trade names all over the world - as patent is still effective.

Sodium-Glucose Transporter Inhibitors

So, this is the newest class of the glucose lowering medications.

And these medicines are approved and introduced in 2014.

Sodium-Glucose Transporter Inhibitors

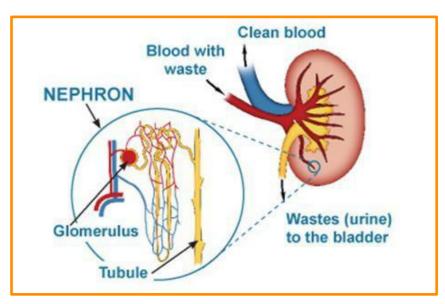
So, this is the newest class of the glucose lowering medications.

And these medicines are approved and introduced in 2014.

The sodium glucose transport channels what we call-

SGLT2 channels/receptors

are present in **proximal tubes of the kidney filtering units.**



Chap2Fig1

SGLT2 channels/receptors

Present in proximal tubes of the kidney filtering units

• <u>SGLT2</u> and <u>SGLT1</u> (Channels/Receptors) does the <u>100%</u> reabsorption of glucose (blood sugar) in filtered urine in kidneys.

SGLT2 & SGLT1 does the 100% REABSORPTION of glucose

• SGLT2 absorb back 90% of the glucose

SGLT2 does the 90% of glucose absorption

• <u>SGLT1</u> does the next <u>10%</u> of the <u>reabsorption</u> of glucose.

SGLT1 does the next 10% of the reabsorption

Role of Selective Sodium-Glucose Transporter-2 (SGLT2) Inhibitors in Diabetes Management

So, all these new medicines "<u>SGLT2</u>" or "Sodium-Glucose Transporter-2 Inhibitors":

- A. Block the sodium glucose transporter tube in the kidneys
- B. And they make kidneys lose sugar in the urine

SGLT2
Sodium-Glucose Transporter-2 Inhibitors

Block the sodium glucose transporter tube in the kidneys

Make kidneys lose sugar in the urine

Without medicine – kidney reabsorb all filtered glucose when blood sugar level is 180mg or less.

C. So, they lower both:

C I) They lower the fasting blood sugar

Lower the Fasting Blood Sugar

C II) And the blood sugar after we eat.

It is called "Postprandial Blood Sugar" (Postprandial means after food).

Lower the Blood Sugar After Eating

D. Since we are losing glucose means we are losing calories.

In other words:

- D (i) We also lose weight, and
- D (ii) These medicines really help in the modest weight loss.



E. While at some level since they are making us lose glucose and along with that some water; and along with water, some sodium also; and sodium is equivalent to salt.

So, they make us lose some salt also and high salt intake is responsible for the high blood pressure. So, they also help us to reduce our blood pressure.

Along with water we lose salt (sodium)

Loss of sodium

reduces blood pressure

Medicines in SGLT2 Inhibitors Group

In the SGLT2 Inhibitors Group, the medicines available in United States are as follows:

There are 4 medicines available in this group:

1. Canagliflozin

(Trade Name: Invokana)



Chap4Fig1

2. Dapagliflozin

(Trade Name: Farixga)



Chap4Fig2

3. Empagliflozin

(Trade Name: Jardiance)



Chap4Fig3

4. Ertugliflozin

(Trade Name: Steglatro)



Chap4Fig3

Canagliflozin

Trade Name: Invokana

Invokana FDA Approval History

FDA Approved: Yes (First approved March 29, 2013)

Brand name: Invokana

Generic name: Canagliflozin

Dosage form: Tablets

Company: Janssen Research & Development, LLC

Treatment for: <u>Diabetes - Type 2</u>, <u>Cardiovascular Risk Reduction</u>, <u>Diabetic Kidney Disease</u>

Canagliflozin

Invokana

Molecular structure of Canagliflozin HO OH OH

Chap5Fig1

What we need to know about Canagliflozin (Invokana):



Chap5Fig2

- I) Canagliflozin (Invokana) reduces blood sugar from 180 mg% to 70 to 90 mg%.
- Reduces blood sugar
- ii) It also <u>reduces HbA1c by almost 1%</u> whether we use it as a monotherapy or the combination of the other oral diabetic medications
- Reduces HbA1c by almost 1%

iii) It also <u>makes us lose about 2 to 5 kg</u> of our body weight

Helps us to lost weight

iv) The <u>maximum dose of Canagliflozin</u> is 100 mg daily

Maximum dose = 100 mg daily

v) It can be increased to 300 mg daily

Dose can be increased to 300 mg daily

Trade Name - Dose - Cost in USA - Cost in India

CANAGLIFLOZIN



Please always combine any blood sugar medicine with diet and exercise

All medicines continue life-long					
Generic Name & Trade Name	About Canagliflozin	Cost of Canagliflozin for one month (in USA)	Cost of Canagliflozin for one month (in India)		
Generic Name: Canagliflozin Trade Name: Invokana (USA)	 Usual dose: 100 mg a day before meal Can be increased to 300 mg daily As a Golden Rule - before starting any 	Dose = 100 mg a day 1 month= \$500 Cost= \$500 for 100 mg 30 tablets	Dose = 100 mg a day 1 month= Rs 1500 Cost= Rs 500 for IO tablets		
Invokana (India)	medicine, liver functions and kidney functions should be screened	*All costs are meant tor a rough estimate of one-month expense.	*All costs are meant for a rough estimate of one-month expense		

Chapter 6

Dapagliflozin Trade Name: Farxiga

Farxiga FDA Approval History

FDA Approved: Yes (First approved January 8, 2014)

Brand name: Farxiga

Generic name: Dapagliflozin

Dosage form: Tablets

Company: AstraZeneca

Treatment for: <u>Diabetes - Type 2</u>

Farxiga (Dapagliflozin) is a sodium-glucose cotransporter 2 (SGLT2) inhibitor indicated

for the treatment of type 2 diabetes mellitus and heart failure.

Dapagliflozin

Farxiga

Chap6Fig1

What we need to know about Dapagliflozin (Farxiga):



Chap6Fig2

- I) Dapagliflozin (Farxiga) reduces HbA1c by 0.5 to 0.8%.
- ii) Roughly the HbA1c gets reduced by 1%. For example: HbA1c 8% will reduce to 7%.
- iii) <u>It can be used alone</u>, or It can be used with <u>other oral blood</u> sugar lowering medications or Insulin
- iv) It can make us lose 2 to 4 kg of weight
- v) It is used 10 mg once daily (we should take it before/with food).

Reduces HbA1c by 0.5 to 0.8%

For example: HbA1c 8% will reduce to 7%.

Can be used alone or with blood sugar lowering medicines

Helps us to lost weight

Maximum dose = 10 mg once daily

Trade Name - Dose - Cost in USA - Cost in India

DAPAGLIFLOZIN

(FARXIGA)

Please always combine any blood sugar medicine with diet and exercise.

All medicines continue life-long					
Generic Name & Trade Name	About Dapagliflozin	Cost of Dapagliflozin for one month (in USA)	Cost of Dapagliflozin for one month (in India)		
Generic Name: Dapagliflozin	usual dose: 10 mg once daily before/ with meal	Dose = 10 mg once daily	Dose = 10 mg once daily		
Trade Name:	■ Can be increased	1 month= \$800	1month = Rs 1800		
Farxiga (USA) Farxiga (India)	alone or with other oral blood sugar lowering medications or insulin	Cost= \$800 for 10 mg 30 tablets	Cost = Rs 1800 for 10 mg 30 tablets		
	Reduces HbAlc by 0.5 to 0.8%				
	■ Can make us lose 2 to 4 kg of weight				
	before starting any medicine, liver functions and kidney functions should be screened.	*All costs are meant for a rough estimate of one-month expense.	*All costs are meant for a rough estimate of one-month expense		

Chapter 7

Empagliflozin Trade Name: Jardiance

Jardiance FDA Approval History

FDA Approved: Yes (First approved August 1, 2014)

Brand name: Jardiance

Generic name: Empagliflozin

Dosage form: Tablets

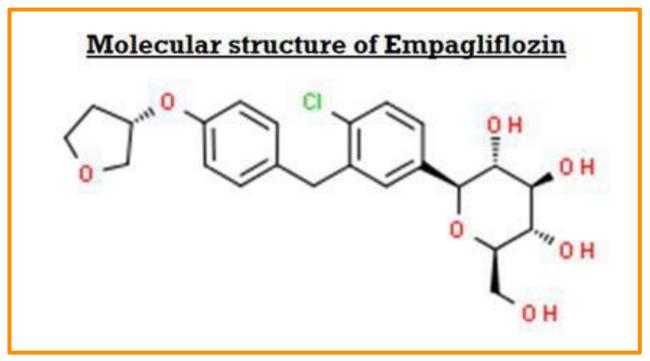
Company: Boehringer Ingelheim Pharmaceuticals, Inc.

Treatment for: <u>Diabetes - Type 2</u>

<u>Jardiance (Empagliflozin)</u> is a sodium glucose co-transporter-2 (SGLT2) inhibitor; along with diet and exercise it improves glycemic control in adults with type 2 diabetes and reduces the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease.

Empagliflozin

Jardiance



Chap7Fig1

What we need to know about Empagliflozin (Jardiance):



Chap7Fig2

- I) Empagliflozin (Jardiance) reduces HbA1c by 0.5 to 0.7%.
- ii) <u>It can be used alone</u>, or It can be used with <u>other oral blood</u> sugar lowering medications
- iii) It can be used with Insulin
- iv) It can make us lose 2 to 3 kg of weight.
- v) It is used <u>10 mg once daily</u> (should take it before/with food). Can be increased up to <u>25 mg once a day.</u>

Reduces HbA1c by 0.5 to 0.7%

Can be used alone or with blood sugar lowering medicines

can be used with Insulin

Helps us to lost weight

Maximum dose = 10 mg once daily

Trade Name - Dose - Cost in USA - Cost in India

EMPAGLIFLOZIN

(JARDIANCE)

Please always combine any blood sugar medicine with diet and exercise.

All medicines continue life-long					
Generic Name & Trade Name	About Empagliflozin	Cost of Empagliflozin for one month (in USA)	Cost of Empagliflozin for one month (in India)		
Generic Name: Empagliflozin	Usual dose: 10 mg once daily before/ with meal	Dose = 10 mg once daily 1 month = \$500	Dose= 10 mg once daily 1 month = Rs 450		
Trade Name:	Can be increased to 25 mg once dailyReduces HbAlc by	Cost= \$500 for 10 mg 30 tablets	Cost= Rs 450 for 10 mg 30 tablets		
Jardiance (India)	0.5 to 0.7% Can make us lose 2 to 3 kg of weight	To To mg So tablets	for rorng so tablets		
_	■ As a Golden Rule - before starting any medicine, liver functions and kidney functions should be screened.	*All costs are meant for a rough estimate of one-month expense.	*All costs are meant for a rough estimate of one-month expense		

Chapter 8

Ertugliflozin

Trade Name: Steglatro

Steglatro FDA Approval History

FDA Approved: Yes (First approved December 19, 2017)

Brand name: Steglatro

Generic name: Ertugliflozin

Dosage form: Tablets
Company: Merck

Treatment for: Diabetes - Type 2

<u>Steglatro (Ertugliflozin)</u> is a sodium-glucose co-transporter-2 (SGLT2) inhibitor used to help improve glycemic control in adults with type 2 diabetes.

Ertugliflozin

Steglatro

Chap8Fig1

What we need to know about Ertugliflozin (Steglatro):



Chap8Fig2

- I) Ertugliflozin (Steglatro) is used 5 mg once daily
- Maximum dose = 5 mg once daily

ii) It can be <u>used alone or with other</u> medications

Can be used with other medicines

- iii)) It can be taken with or without food
- Can be taken with or without food
- iv) It can be increased to 15 mg once daily.
- Dose can be increased to 15 mg once daily

Trade Name - Dose - Cost in USA - Cost in India

ERTUGLIFLOZIN

(STEGLATRO)

Please always combine any blood sugar medicine with diet and exercise.

All medicines continue life-long Cost of Ertugliflozin **Cost of Ertugliflozin** Generic Name & About for one month for one month Trade Name Ertugliflozin (in USA) (in India) ■ Usual dose: 5 mg by Dose = 5 mg onceDose = 5 mg once**Generic Name:** mouth every day daily daily (once daily before/ **Ertugliflozin** with meal) $1 \, \text{month} = \$350$ 1 month = Rs 600**Trade Name:** ■ Can be increased **Cost=** \$350 Cost= Rs 600 to 15 mg by mouth Steglatro (in USA) every day (once for 5 mg 30 tablets for 5 mg 30 tablets Steglujan (in India) daily before/with meal) Cost of one tablet in USA is approximately \$12 As a Golden Rule -*All costs are meant *All costs are meant before starting any for a rough estimate for a rough estimate medicine, liver of one-month of one-month expense functions and kidney expense. functions should be screened.

Chapter 9

Important Facts About These Medications

These are excellent medicines, a little costly, but effective.

Let us review one more time - medical facts which all of us should know.

Fact #1 - Dehydration:

- Since they make us lose glucose in the urine,
- And, along with the glucose goes the water,
- So, we pee a lot,
- And, we have to **drink lot of water**,
- Or we are at the <u>risk of getting dehydrated</u>.

These medicines increase the risk of DEHYDRATION

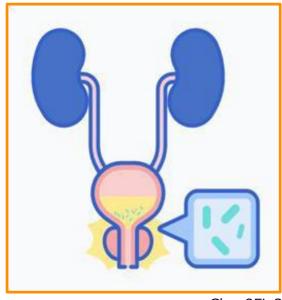


Chap9Fig1

Fact #2 - UTI

- In the women, there is a risk of developing the **yeast infection.**
- Because of the <u>increased glucose in</u> the urine.
- Or urinary tract infection (UTI)
- Just because of the <u>increased glucose</u>
 <u>In the urine.</u>
- So, women really need to <u>maintain</u> <u>flow of urine.</u>
- In other words, <u>drink lot of water</u> with good access to washrooms/rest rooms

These medicines increase the risk of YEAST INFECTION & UTI



Chap9Fig2

"We obviously need normal kidney functions for these medications to work."

Loss of Water Loss of Glucose

Urinart Tract Infection (UTI) Genital Infection (with yeast)

Increased Water Loss in Urine Dehydration Loss of Glucose

FACT - Increased urinary frequency:

So, these medications lead to increased urinary frequency.

I mean going to bathroom again and again because of the increased glucose and losing lot of water along with it.

• FACT - UTI:

Then, there may be <u>lower urinary tract infection (UTI)</u> because of the increased glucose in urine.

It is less common in men and more common in women, just because of gender anatomy.

• FACT - Genital Infection/Yeast Infection:

There may be **genital infection** with the yeast because of glucose in urine, but very easy to manage just with one pill.

• Fact - Dehydration:

- Since they make us <u>lose glucose in the</u> <u>urine</u>,
- And, along with the glucose goes the water,
- So, we pee a lot,
- And, we have to drink lot of water,
- Or we are at the <u>risk of getting</u> dehydrated.

These medicines increase the risk of <u>DEHYDRATION</u>



Chap9Fig3

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- And, along with the glucose goes the water,
- So, we pee a lot.
- And, we have to drink lot of water,
- Or we are at the <u>risk of getting</u> <u>dehydrated</u>.

These medicines increase the risk of <u>DEHYDRATION</u>



Chap9Fig3

It can lead to **dehydration** also as we are losing lot of glucose and water in the urine.

Usually, urinary tract infection (UTI) and yeast infection are much less common in men. They are more common in women.

Also, it is for them to drink plenty of water and maintain good urine flow

So, what should we do?

My recommendations as a medicine doctor, kidney doctor and diabetes doctor:

Recommendation #1:

As a golden rule, we should always maintain:2 liters of urine outflow

It does not matter whether we drink 5 liters.

The reason is in summer we lose so much water from lungs and skin to keep skin cool and to keep air in lungs moisturized (dry air is very irritative and cough producing)

Drink plenty of water/
fluids: Tea Coffee Regular/
diet coke Juices
Homemade drinks



Chap9Fig4

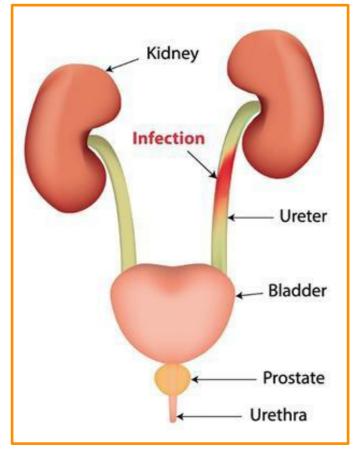
Recommendation #2:

Please always **seek treatment** whenever there are symptoms.

"Young girls and women all should learn basics of UTI and yeast infection as it is/can be very common, but very easy to treat."

They are at high risk:

- During monthly cycle
- Dehydration
- After being intimate
- After marriage
- After any gynae procedure



Chap9Fig5

Think About It!

"As a kidney doctor I have seen patients where due to delayed treatment, infection going to kidneys and it becomes serious and urgent to treat. If delayed further, it goes to blood – then even in 2021 - risk of survival is 50:50."

Good flow of urine will be very-very helpful – but that is exactly what young girls and women in India avoid – just because of lack of access to good hygienic washrooms.

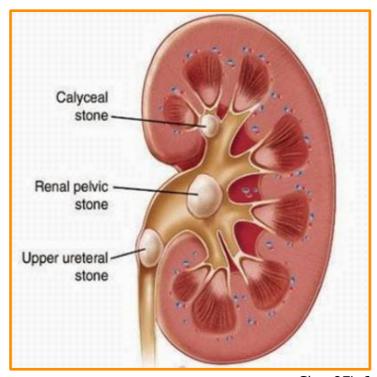
Think About It!

"This is a kidney stone experience of one of my patients. He had terrible kidney stone pain and the worst thing was he had them 5 times!!

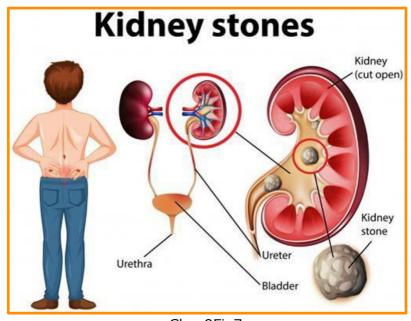
For the simple reason that he did not know what was happening to him & it was very frightening having all that pain & no position that he would put himself into would help it.

He was taken to the hospital where he had X rays & was put onto a drip just for fluids & given an injection of morphine & an anti-inflammatory which worked after about 35 mins. The pain relief was so good that he fell asleep immediately & woke up in the hospital ward, the next morning where he passed the stone.

When he got the same pain again, he was in a lot of pain but not frightened as I knew. Fortunately, after being prescribed Allopurinol he has had no recurrence, fingers crossed."



Chap9Fig6



Chap9Fig7

So, it is your choice – please take medicine in morning or when you get home.

You may want to avoid before sleep – as going to washroom may interrupt your sleep.



Seek treatment when symptoms arise

Chap9Fig8



Chap9Fig9