A COMPREHENSIVE REVIEW ON NOVEL ANTIDIABETIC AND ANTIHYPERTENSIVE DRUGS

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ABSTRACT

Diabetes mellitus is a common form of metabolic disorder where level of blood glucose in the bloodstream raises high, because of deficiency of insulin and development of insulin resistance in diabetic individuals. It is categorize under modern age life style disorder, commonly affected by middle-aged people and the children in adolescents in most developed countries. Diabetic patients develop serious complication with the development of disease, such as obesity, risk of stroke and heart failure. Globally antidiabetic drugs formulate the second-largest market by sales in the pharmaceuticals industry after cancer. Various novel targets have identified and recently various therapeutic leads successfully completed their different phases of clinical trials such as GLP-1 agonist, DPP-IV inhibitors, SGLT2 inhibitors, and are going to be the next generation therapy for management of diabetes.

Hypertension is the medical term for high blood pressure. It is dangerous because it makes the heart work too hard and contributes to atherosclerosis (hardening of arteries), besides increasing the risk of heart disease and stroke. HTN can also lead to other conditions such as congestive heart failure, kidney disease and blindness. Conventional antihypertensives are usually associated with many side effects. About 75 to 80% of the world population use herbal medicines, mainly in developing countries, for primary health care because of their better acceptability with human body and lesser side effects.

KEYWORDS: Diabetes, GLP1 agonist, DPP4 Inhibitors, SGLT2 Inhibitors, Hypertension, Herbal drugs, Antihypertensive, Atherosclerosis.

INTRODUCTION

Diabetes Mellitus is a metabolic disorder characterized by the presence of chronic hyperglycemia accompanied by greater or lesser impairment in the metabolism of
carbohydrates, lipids and proteins. DM is probably one of the oldest diseases known to man. It was first reported in Egyptian manuscript about 3000 years ago.\[^1\] In 1936, the distinction between type 1 and type 2 DM was clearly made.\[^2\] Type 2 DM was first described as a component of metabolic syndrome in 1988.\[^3\] The origin and etiology of DM can vary greatly but always include defects in either insulin secretion or response or in both at some point in the course of disease. Mostly patients with diabetes mellitus have either type 1 diabetes (which is immune-mediated or idiopathic) Type 2 DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency.\[^4\] Type 2 DM results from interaction between genetic, environmental and behavioral risk factors.\[^5\] Diabetes also can be related to the gestational hormonal environment, genetic defects, other infections, and certain drugs.\[^6\]

In modern age medicine, treatments are available for diabetes like Sulfonylureas, GLP-1 agonist, DPP4 inhibitors, metformin, PPAR-\(\gamma\) agonists, pioglitazone and rosiglitazone, GPR119 agonists, bariatric surgery etc. and some recent therapies are available like SGLT2 inhibitors.

**Type 1 diabetes mellitus:** Type 1 diabetes mellitus (juvenile diabetes) is characterized by beta cell destruction caused by an autoimmune process, usually leading to absolute insulin deficiency.\[^6\] Type 1 is usually characterized by the presence of anti–glutamic acid decarboxylase, islet cell or insulin antibodies which identify the autoimmune processes that lead to beta cell destruction. Eventually, all type1 diabetic patients will require insulin therapy to maintain normal glycemia.

**Type 2 diabetes mellitus:** The relative importance of defects in insulin secretion or in the peripheral action of the hormone in the occurrence of DM2 has been and will continue to be cause for discussion. DM2 comprises 80% to 90% of all cases of DM. Most individuals with Type 2 diabetes exhibit intra-abdominal (visceral) obesity, which is closely related to the presence of insulin resistance. In addition, hypertension and dyslipidemia (high triglyceride and low HDL-cholesterol levels; postprandial hyperlipidemia) often are present in these individuals. This is the most common form of diabetes mellitus and is highly associated with a family history of diabetes, older age, obesity and lack of exercise.\[^6\] Hypertension is a chronic condition characterised by a sustained diastolic reading greater than or equal to 80 mmHg and a systolic reading greater than or equal to 120 mmHg (120/80 mmHg). Hypertension or high blood pressure is widely prevalent and a major risk factor for
cardiovascular diseases including coronary heart disease, myocardial infraction and stroke, and frequently causes damage to the arterial blood vessels, the eyes and kidneys. Prolonged hypertension can also lead to enlargement of the heart and may cause heart failure. This disease is usually asymptomatic until the damaging effects of hypertension are observed. Therefore, hypertension is known as the “silent killer”.

What constitutes “hypertension?”

Abnormally high blood pressure is generally divided into two main categories: essential hypertension and secondary hypertension. Essential or primary hypertension is the most prevalent type, affecting between 90-95 present of patients diagnosed with hypertension. It is not an easy task to choose among the various categories. In coming to a sound decision, the physician way take several courses, approaching the problem from a drug-related or a patient-related perspective.[7-8]

DRUGS USED IN DIABETIS

Tresiba (insulin degludec injection)
Company: Novo Nordisk, Approval Status: Approved September 2015
Specific Treatments: glycemic control in adults with diabetes mellitus

General Information
Tresiba (insulin degludec) is a long-acting human insulin analog.

Tresiba is specifically indicated to improve glycemic control in adults with diabetes mellitus. Tresiba is supplied as an injection for subcutaneous administration. Inject Tresiba subcutaneously once-daily at any time of day into the thigh, upper arm, or abdomen. Rotate injection sites within the same region from one injection to the next to reduce the risk of lipodystrophy. Individualize and titrate the dose of Tresiba based on the patient’s metabolic needs, blood glucose monitoring results, and glycemic control goal. The recommended days between dose increases is 3 to 4 days.[9-11]

Ozempic (semaglutide)
Company: Novo Nordisk.
Approval Status: Approved December 2017.
Specific Treatments: type II diabetes.
**General Information:** Ozempic (semaglutide) is a glucagon-like peptide 1 (GLP-1) receptor agonist. Ozempic is specifically indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Ozempic is supplied as a solution for subcutaneous injection into the abdomen, thigh or upper arm. The recommended starting dose is 0.25 mg once weekly. After 4 weeks, the dose should be increased to 0.5 mg once weekly. If after at least 4 weeks additional glycemic control is needed, increase the dose to 1 mg once weekly. Ozempic should be administered once weekly at any time of day, with or without meals. If a dose is missed administer within 5 days of missed dose.\textsuperscript{[12]}

**Adlyxin (lixisenatide)**

**Company:** Sanofi Aventis, **Approval Status:** Approved July 2016

**Specific Treatments:** type II diabetes

**General Information**

Adlyxin (lixisenatide) is a once-daily glucagon-like peptide-1 receptor agonist (GLP-1 RA). GLP-1 is a peptide hormone that is released within minutes after eating a meal. It is known to suppress glucagon secretion from pancreatic alpha cells and stimulate glucose-dependent insulin secretion by pancreatic beta cells. Adlyxin increases glucose-dependent insulin release, decreased glucagon secretion, and slows gastric emptying. Adlyxin is specifically indicated as an adjunct to diet and exercise for the treatment of adults with type II diabetes. Adlyxin is supplied in a disposable pre-filled pen in a single dose of 20 micrograms for subcutaneous administration. Patients will also receive a disposable pre-filled pen in a single dose of 10 micrograms that they should initiate once daily for 14 days. On Day 15, patients should increase dosage to 20 micrograms once daily.\textsuperscript{[13]}

**Bydureon (exenatide extended-release for injectable suspension)**

**Company:** Amylin, **Approval Status:** Approved January 2012

**Specific Treatments:** glycemic control in adults with type II diabetes mellitus

**General Information:** Bydureon is an extended-release formulation of exenatide, a GLP-1 receptor agonist that enhances glucose-dependent insulin secretion by the pancreatic beta-cell, suppresses inappropriately elevated glucagon secretion, and slows gastric emptying. Bydureon is specifically indicated as an adjunct to diet and exercise to improve glycemic
control in adults with type II diabetes mellitus in multiple clinical settings. Bydureon is supplied as a powder suspension to be reconstituted into a solution. The recommended dose is 2 mg administered once every seven days (weekly). The dose can be administered at any time of day, with or without meals. Bydureon is administered as a subcutaneous (SC) injection in the abdomen, thigh or upper arm region.\[14\]

**Nesina (alogliptin)**

![Nesina molecule](image)

**Company:** Takeda, **Approval Status:** Approved January 2013.

**Specific Treatments:** type II diabetes mellitus.

**General Information**

Nesina (alogliptin) is a small-molecule, orally available dipeptidyl peptidase IV (DPP IV) inhibitor. DPP-4 inhibitors slow the inactivation of incretin hormones GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulino tropic peptide), both of which play a role in regulating blood glucose levels. Nesina is specifically indicated as an adjunct to diet and exercise to improve glycemic control in adults with type II diabetes mellitus. Nesina is supplied as a tablet for oral administration. The recommended dose is 25 mg once daily, with or without food.\[15\]

**Juvisync (sitagliptin and simvastatin)**
**Company:** Merck, **Approval Status:** Approved October 2011

**Specific Treatments:** type II diabetes

**General Information:** Juvisync is a single tablet combination of the glucose-lowering medication sitagliptin, the active component of Januvia, with the cholesterol-lowering medication simvastatin, the active component of Zocor. Juvisync is specifically indicated for the treatment of type II diabetes in patients for whom treatment with both sitagliptin and simvastatin is appropriate. Juvisync is supplied as a tablet for oral administration. The recommended initial dose is 100 mg/40 mg per day. For patients already taking simvastatin (10, 20, or 40 mg daily) with or without sitagliptin 100 mg daily, Juvisync may be initiated at the dose of 100 mg sitagliptin and the dose of simvastatin already being taken.[16]

**Steglatro (ertugliflozin)**

**Company:** Merck, **Approval Status:** Approved December 2017

**Specific Treatments:** type 2 diabetes mellitus

**General Information**

Steglatro (ertugliflozin) is a sodium glucose co-transporter 2 (SGLT2) inhibitor. Steglatro is specifically indicated as an adjunct to diet and exercise to improve glycemic control in adults with type II diabetes mellitus. Steglatro was also approved for use in combination with sitagliptin and in combination with metformin. Steglatro is supplied as a tablet for oral administration. The recommended starting dose is 5 mg once daily, taken in the morning, with or without food. In patients tolerating 5 mg once daily, the dose may be increased to a maximum recommended dose of 15 mg once daily if additional glycemic control is needed. Please see drug label for administration in patients with renal impairment.[17]
Synjardy (empagliflozin and metformin hydrochloride)

Company: Boehringer Ingelheim, Approval Status: Approved August 2015
Specific Treatments: type II diabetes.

General Information: Synjardy is a combination of empagliflozin and metformin, two medicines with complementary mechanisms of action. Empagliflozin, a sodium glucose co-transporter-2 (SGLT2) inhibitor, removes excess glucose through the urine by blocking glucose re-absorption in the kidney. Metformin lowers glucose production by the liver and its absorption in the intestine. Synjardy is specifically indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are not adequately controlled on a regimen containing empagliflozin or metformin, or in patients already being treated with both empagliflozin and metformin.\(^{[18]}\)

Farxiga (dapagliflozin)

Company: Bristol-Myers Squibb, Approval Status: January of 2014.
Specific Treatments: type II diabetes.
General Information: Farxiga (dapagliflozin) is an orally active sodium glucose cotransporter type 2 (SGLT-2) inhibitor. Inhibiting SGLT2 activity modulates reabsorption of glucose in the kidney, resulting in excretion of glucose in the urine. Farxiga is specifically indicated as an adjunct to diet and exercise to improve glycemic control in adults with type II diabetes mellitus. Farxiga is supplied as a tablet for oral administration. The recommended starting dose is 5 mg once daily, taken in the morning, with or without food. The dose can be increased to 10 mg once daily in patients tolerating Farxiga who require additional glycemic control. Renal function should be assessed before initiating Farxiga.\textsuperscript{[19]} Jardiance (empagliflozin).

Company: Boehringer Ingelheim, Approval Status: Approved August 2014
Specific Treatments: type II diabetes

General Information
Jardiance (empagliflozin) is a sodium-glucose co-transporter 2 (SGLT2) inhibitor. Jardiance is specifically indicated as an adjunct to diet and exercise to improve glycemic control in adults with type II diabetes mellitus. Jardiance is supplied as a tablet for oral administration. The recommended dose is 10 mg once daily in the morning, taken with or without food. In patients tolerating Jardiance, the dose may be increased to 25 mg.\textsuperscript{[20]}

Xigduo XR (dapagliflozin + metformin hydrochloride)
Company: AstraZeneca, Approval Status: Approved October 2014
Specific Treatments: glycemic control in adults with type II diabetes

General Information
Xigduo XR is a combination of dapagliflozin, an inhibitor of sodium-glucose cotransporter 2 (SGLT2), and metformin hydrochloride extended-release, a biguanide. SGLT2 inhibitors remove glucose from the body via the kidneys.

Xigduo XR is specifically indicated as an adjunct therapy to diet and exercise to improve glycemic control in adults with type II diabetes mellitus when treatment with both dapagliflozin and metformin is appropriate. Xigduo XR is supplied as a tablet for oral administration. The starting dose should be individualized based on each patient’s current treatment regimen. The maximum daily recommended dose is 10 mg for dapagliflozin and 2,000 mg for metformin HCl. Xigduo XR should be taken once daily in the morning with food with gradual dose escalation to reduce the risk of gastrointestinal side effects due to metformin.[21]

Invokana (canagliflozin)

Company: Janssen Pharmaceuticals.
Approval Status: Approved April 2013.
Specific Treatments: type II diabetes mellitus.

General Information
Invokana (canagliflozin) is a sodium-glucose co-transporter 2 (SGLT2) inhibitor. Inhibiting SGLT2 is believed to reduce blood glucose levels by increasing the amount of glucose excreted in the urine. Invokana is specifically indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus/ Invokana is supplied as tablets for oral administration. The recommended starting dose of Invokana is 100 mg once
daily, taken before the first meal of the day. In patients tolerating Invokana 100 mg once
daily who have an eGFR of 60 mL/min/1.73 m2 or greater and require additional glycemic
control, the dose can be increased to 300 mg once daily.\textsuperscript{[22]}

\textbf{Qtern (dapagliflozin and saxagliptin)}

\textbf{Company:} AstraZeneca.
\textbf{Approval Status:} Approved February 2017
\textbf{Specific Treatments:} inadequately controlled type II diabetes

\textbf{General Information}
Qtern combines two antihyperglycemic agents: dapagliflozin, a sodium-glucose
cotransporter2 (SGLT-2) inhibitor, and saxagliptin, a dipeptidyl peptidase-4 (DPP-4)
inhibitor. Qtern is specifically indicated as an adjunct to diet and exercise to improve
glycemic control in adults with type 2 diabetes mellitus (T2DM) who have inadequate control
with dapagliflozin or who are already treated with dapagliflozin and saxagliptin.\textsuperscript{[23]}

\textbf{Afrezza}
\textbf{Company:} Mannkind.
\textbf{Approval Status:} Approved June 2014
\textbf{Specific Treatments:} diabetes mellitus

\textbf{General Information}
Afrezza is a rapid acting inhaled insulin powder. When the insulin is inhaled through
the device, the powder is aerosolized and delivered to the lung. Afrezza is specifically
indicated to improve glycemic control in adult patients with diabetes mellitus.\textsuperscript{[24]}
**Herbal Antidiabetic Drugs.**^{25-27}

<table>
<thead>
<tr>
<th>Plant Name</th>
<th>Ayurvedic/common name/herbal formulation</th>
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<tbody>
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<td>Davana</td>
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<tr>
<td>Areca catechu</td>
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<td>Chukkander</td>
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<td>Punarnava</td>
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<td>Capparis decidua</td>
<td>Karir or Pinju</td>
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<td>Caesalpinia bonduncella</td>
<td>Sagarghota, Fevernut</td>
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<tr>
<td>Coccinia indica</td>
<td>Bimb or Kanturi</td>
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<td>Amla, Dhatriphala, a constituent of herbal formulation, “Triphala”</td>
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<td>Hibiscus rosa-sinensis</td>
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<td>Curry patta</td>
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<tr>
<td>Musa sapientium</td>
<td>Banana</td>
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<tr>
<td>Phaseolus vulgaris</td>
<td>Hulga, white kidney bean</td>
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<td>Salaciarenticulata</td>
<td>Vairi</td>
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<td>Sweet broomweed</td>
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<td>Chirata</td>
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<td>Syzygium alternifolium</td>
<td>Shahajire</td>
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<tr>
<td>Terminalia belerica</td>
<td>Behada, a constituent of “Triphala”</td>
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<tr>
<td>Terminalia chebula</td>
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<tr>
<td>Tinospora crispa</td>
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<tr>
<td>Withania somnifera</td>
<td>Ashvagandha, winter cherry</td>
</tr>
</tbody>
</table>

**Drugs Used In Hypertension**

**Byvalson (nebivolol and valsartan)**

Specific Treatments: hypertension.

General Information: Byvalson (nebivolol and valsartan 5 mg/ 80 mg tablet) is a fixed-dose combination of nebivolol - a beta-adrenergic receptor blocking agent that is preferentially beta-1 selective, and valsartan - an angiotensin II receptor blocker. Byvalson is specifically indicated for the treatment of hypertension, to lower blood pressure. Byvalson is supplied as a tablet for oral administration. The recommended dose is as follows: as initial therapy and in patients not adequately controlled on valsartan 80 mg or nebivolol up to and including 10 mg, the recommended dose is 5 mg/ 80 mg taken orally once daily. Maximum antihypertensive effects are attained within 2 to 4 weeks. Byvalson may be substituted for its components in patients already receiving 5 mg nebivolol and 80 mg valsartan.\(^{28}\)

Opsumit (macitentan)


Specific Treatments: pulmonary arterial hypertension.

General Information

Opsumit (macitentan) is a tissue-targeting Endothelin Receptor Antagonist. Endothelin Receptor Antagonists mediate a variety of deleterious effects, such as vasoconstriction, fibrosis, proliferation, hypertrophy, and inflammation. Opsumit is specifically indicated for the treatment of pulmonary arterial hypertension (WHO Group I) to delay disease progression. Opsumit is supplied as a tablet for oral administration. The recommended dose is 10 mg once daily.\(^{29}\)
Prestalia (perindopril arginine and amlodipine besylate)

**Company:** Symplmed Pharmaceuticals, **Approval Status:** Approved January 2015, **Specific Treatments:** hypertension.

**General Information:** Prestalia is a combination of perindopril, an angiotensin converting enzyme (ACE) inhibitor, and amlodipine, a dihydropyridine calcium channel blocker. Prestalia is specifically indicated for the treatment of hypertension, to lower blood pressure in patients not adequately controlled with monotherapy and as initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals. Prestalia is supplied as a tablet for oral administration. The recommended starting oral dose of Prestalia is 3.5/2.5 mg once daily. The dose may be adjusted according to blood pressure goals waiting 1 to 2 weeks between titration steps. The maximum recommended dose is 14/10 mg once daily.\[30,31\]

Uptravi (selexipag)

**Company:** Actelion Pharmaceuticals, **Approval Status:** Approved December 2015, **Specific Treatments:** pulmonary arterial hypertension.

**General Information**

Uptravi (selexipag) is a prostacyclin receptor agonist, which exerts vasodilating effects. Uptravi is specifically indicated for the treatment of pulmonary arterial hypertension (PAH,
WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH. Uptravi is supplied as tablets for oral administration. The recommended starting dose of Uptravi is 200 micrograms (mcg) given twice daily. Tolerability may be improved when taken with food. The dose should be increased in increments of 200 mcg twice daily, usually at weekly intervals, to the highest tolerated dose up to 1600 mcg twice daily. If a patient reaches a dose that cannot be tolerated, the dose should be reduced to the previous tolerated dose. Do not split, crush, or chew tablets.[32]

**Adempas (riociguat)**

Company: Bayer Healthcare Pharmaceuticals, Approval Status: Approved October 2013, Specific Treatments: Chronic Thromboembolic Pulmonary Hypertension and Pulmonary Arterial Hypertension.

General Information: Adempas (riociguat) is a stimulator of soluble guanylatecyclase (sGC), an enzyme in the cardiopulmonary system and the receptor for nitric oxide (NO). These stimulators help arteries relax to increase blood flow and decrease blood pressure. Adempas is specifically indicated for persistent/recurrent Chronic Thromboembolic Pulmonary Hypertension (CTEPH) (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class and Pulmonary Arterial Hypertension (PAH) (WHO Group 1) to improve exercise capacity, improve WHO functional class and to delay clinical worsening.[33] Adempas is supplied as a tablet for oral administration. The recommended initial dose is 1 mg taken three times a day. For patients who may not tolerate the hypotensive effect of Adempas, consider a starting dose of 0.5 mg, three times a day. The dose may be increased by 0.5 mg at intervals of no sooner than 2-weeks as tolerated to a maximum of 2.5 mg three times a day.[34]
Edarbi (azilsartanmedoxomil)

General Information
Edarbi (azilsartanmedoxomil), a prodrug, is hydrolyzed to azilsartan in the gastrointestinal tract during absorption. Azilsartan is a selective AT1 subtype angiotensin II receptor antagonist. It's mechanism of action is to lower blood pressure by inhibiting action of vasopressor hormone Angiotensin II, a polypeptide that causes vasoconstriction, increased blood pressure and aldosterone release. Edarbi is specifically indicated for the treatment of hypertension, alone or in combination with other antihypertensive agents.

Edarbi is supplied as a tablet for oral administration. The recommended initial dose in adults is 80 mg taken orally once daily.\(^{[35]}\)

Edarbyclor (azilsartanmedoxomil and chlorthalidone)

Company: Takeda, Approval Status: Approved December of 2011.
Specific Treatments: hypertension.
**General Information:** Edarbyclor is a fixed dose combination of azilsartanmedoxomil, an angiotensin II receptor blocker, and the diuretic chlorthalidone. The sodium and water depletion action of chlorthalidone appear to provide a basis for its antihypertensive effect. Edarbyclor is specifically indicated for the treatment of hypertension, to lower blood pressure in the following populations: those not adequately controlled with monotherapy and as initial therapy in patients likely to need multiple drugs to help achieve blood pressure goals. Edarbyclor is supplied as a tablet for oral administration. The recommended starting dose of Edarbyclor is 40/12.5 mg taken orally once daily. The dosage may be increased to 40/25 mg after 2 to 4 weeks as needed.\[^{36}\]

**Adcirca (tadalafil)**

![Adcirca (tadalafil) molecule](image)

**Company:** Eli Lilly, **Approval Status:** Approved May 2009.  
**Specific Treatments:** pulmonary arterial hypertension

**General Information:** Adcirca (tadalafil) is an oral inhibitor of phosphodiesterase type 5 (PDE5), the enzyme responsible for the degradation of cyclic guanosine monophosphate (cGMP). Pulmonary hypertension is the result of upregulation of PDE5 gene expression, causing vasoconstriction in the lung. Inhibition of PDE5 by tadalafil increases the concentrations of cGMP resulting in relaxation of pulmonary vascular smooth muscle cells and vasodilation of the pulmonary vascular bed.\[^{37}\] Adcirca is specifically indicated for the treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability. Adcirca is supplied as a 20 mg tablet for oral administration. The recommended initial dose of the drug is 40 mg (two 20 mg tablets) taken once daily with or without food. Dividing the dose (40 mg) over the course of the day is not recommended.\[^{38}\]
Tiazac (diltiazem hydrochloride)

Company: Forest Laboratories, Approval Status: Approved February 1996
Specific Treatments: hypertension.

General Information: Tiazac has been approved as a treatment for hypertension. The once-daily calcium channel blocker reduces blood pressure of hypertensive subjects. Through its extended-release, osmotic diffusion system of concentrated diltiazem beads, Tiazac delivers smooth 24-hour plasma levels, which are highly correlated with blood pressure measurements. When properly dosed, Tiazac provides smooth and predictable 24-hour blood pressure control. A greater blood pressure reduction is achieved with Tiazac when blood pressure is at its highest, yet Tiazac achieves blood pressure reduction without causing hypotension during periods of lower blood pressure. Tiazac, a highly concentrated formulation of diltiazem, enables more drug to be contained inside a smaller capsule. This formulation allows for both smaller capsules for a given dosage, relative to the same dose of other once-daily diltiazem products, and for five dosage strengths: 120, 180, 240, 300, and 360 mg.

Tiazac, as with all diltiazem formulations, should not be used in subjects with severe hypotension (less than 90 mm Hg systolic), acute myocardial infarction and pulmonary congestion documented by x-ray on admission, subjects with sick sinus syndrome or 2nd/3rd-degree AV block (unless used with a pacemaker), and subjects who have demonstrated hypersensitivity to the drug. This drug should be used with caution in subjects with impaired kidney, liver, or heart function.\[^{39}\]

Herbal drugs: Natural products from plants, animals, and minerals have been the basis of the treatment of human disease. Today estimate that about 80% of people in developing countries still relays on traditional medicine based largely on species of plants and animals for their
primary health care. Herbal medicines are currently in demand and their popularity is increasing day by day. About 500 plants with medicinal use are mentioned in ancient literature and around 800 plants have been used in indigenous systems of medicine. India is a vast repository of medicinal plants that are used in traditional medical treatments. There has been an increase in demand for the Phytopharmaceutical products of Ayurveda in Western countries, because of the fact that the allopathic drugs have more side effects. Many pharmaceutical companies are now concentrating on manufacturing of herbal and Phytopharmaceutical products. In India, around 20,000 medicinal plants have been recorded. Chemical principles from natural sources have become much simpler and have contributed significantly to the development of new drugs from medicinal plants.\cite{40}

**Ayurvedic medicines used in management of high blood pressure.**

<table>
<thead>
<tr>
<th>Sarpagandha powder</th>
<th>1000mg</th>
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</thead>
<tbody>
<tr>
<td>Ashwagandha powder</td>
<td>1000mg</td>
</tr>
<tr>
<td>Pippali powder</td>
<td>125mg</td>
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</tbody>
</table>

**DOSAGE:** Take this mixture with ½ teaspoon cows ghee, arm milk and along with 5 soaked almonds. you should take it twice daily. The best time to take this mixture is before 6 AM in the morning and before 6 PM in the evening.

<table>
<thead>
<tr>
<th>Nilofar (waterlily) flowers powder</th>
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<tr>
<td>Sarpagandha</td>
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<tr>
<td>Jaharmohra Khatai Pishti</td>
<td>500 mg</td>
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<tr>
<td>Praval Pishti</td>
<td>500 mg</td>
</tr>
<tr>
<td>Mukta Pishti</td>
<td>125 mg</td>
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</tbody>
</table>

**DOSAGE:** Take this mixture with a cup of KalchiLassi, SharbatGulab or Rose water. You should take it twice daily. The best time to take this mixture is before 10 AM in the morning and before 10 PM in the evening.

<table>
<thead>
<tr>
<th>Sarpagandha Powder</th>
<th>1000mg</th>
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<td>Khurasani Ajwain (Henbane) powder</td>
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<tr>
<td>Tamara Bhasma</td>
<td>10mg</td>
</tr>
</tbody>
</table>

**Dosage:** Take this mixture ½ teaspoon of honey. If you are diabetic, then you can take it with warm ater. You should take it twice daily. The best time to take this mixture is before 8AM in the morning and before 8PM in the evening.\cite{41,42}
CONCLUSION

As diabetic mellitus is a life threatening disease, it is mandatory to get information about its treatment which is other than insulin injection. As taking the treatment of an insulin injection, it is very difficult and inconvenience to the patient as well as it is painful. Hence by using these drugs we can inhibit the increasing level of glucose in the body. As these drugs are administered by oral route it is very comfortable to patient to carry the dosage form as well as it is very easy or administration.

As a hypertension is dangerous because it makes the heart work too hard and contributes to atherosclerosis (harding of arteries), besides increase the risk of heart disease stroke. It is mandatory to get information about its treatment. As taking the treatment of an hypertension is very difficult and inconvenience. Hence by using this drug we can inhibit the increasing level of blood pressure in the body.

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