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Review on Analytical Method Development and Validation for Evogliptin Tartrate and Metformin Hydrochloride

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ABSTRACT

Type 2 diabetes mellitus (T2DM) has also increased in 2019 (27.35 deaths per 100,000) as of 1990 (23.30 deaths per 100,000). The use of Evogliptin, a dipeptidyl peptidase-IV (DPP-IV) inhibitor, has been used for the treatment of T2DM in the last two decades. Metformin is a biguanide antihyperglycemic agent and first-line pharmacotherapy used for T2DM. The broad utilization of metformin has also allowed epidemiological observations. For the estimation of single and simultaneous methods of Evogliptin tartrate and metformin hydrochloride using HPLC, HPTLC, and UV Spectrophotometric methods were reported. So, this review can be used for the further analysis of Evogliptin tartrate and metformin hydrochloride.

INTRODUCTION

1. INTRODUCTION OF DIABETES MELLITUS

Diabetes mellitus (DM) is a metabolic ailment that causes excessive blood sugar in the blood. (DM), generally called diabetes, is a set of metabolic issues characterized by way of an excessive blood sugar stage over a prolonged period of time.

The Chronic Hyperglycemia of diabetes is associated with lengthy-time period damage, disorder, and failure of numerous organs, particularly the eyes, kidneys, nerves, coronary heart, and blood vessels. [1]

♦ Symptoms:

Weight loss**,** Polyuria (frequent urination)**,** Polydipsia (increased thirst)**,** Polyphagia (increased appetite)

♦ Complication:

Diabetic ketoacidosis. Hyperosmolar hyperglycemic nation, Death, Cardiovascular ailment, Stroke, Chronic kidney disorder, Foot ulcers, Damage to nerves, Damage to eyes, Cognitive impairment

♦ Two major types of diabetes mellitus are:

Type I

Insulin-dependent diabetes mellitus (IDDM), juvenile-onset diabetes mellitus:

There is beta cell destruction in pancreatic islets and the majority of the cases are autoimmune (type 1A), antibodies that destroy beta cells are detectable in blood, but some are idiopathic (type 1B) where no antibody is found.

Type II

Non-insulin-dependent diabetes mellitus (NIDDM), maturity-onset diabetes mellitus:

There is no loss or moderate reduction in beta cell mass, insulin in circulation is low, normal or even high, no anti-beta-cell antibody is demonstrable; has a high degree of genetic

predisposition; generally, has a late onset (past middle age). Over 90% cases are type 2 DM.[2]

♦ Adverse consequences:

1. Gastrointestinal troubles – along with nausea, diarrhea and belly ache.
2. Flu-like signs – headache, runny nose, sore throat.
3. Skin reactions – painful skin accompanied by way of a red or pink rash.[3]

♦ Oral medication:

Sometimes blood sugar levels remain high in people with type 2 diabetes even though they eat in a healthy manner and exercise.

Example: Metformin, Sulfonylureas, Meglitinides, Thiazolidinediones, Dpp-4 inhibitors, GLP-1 receptor agonists. [4] (Fig. 1).

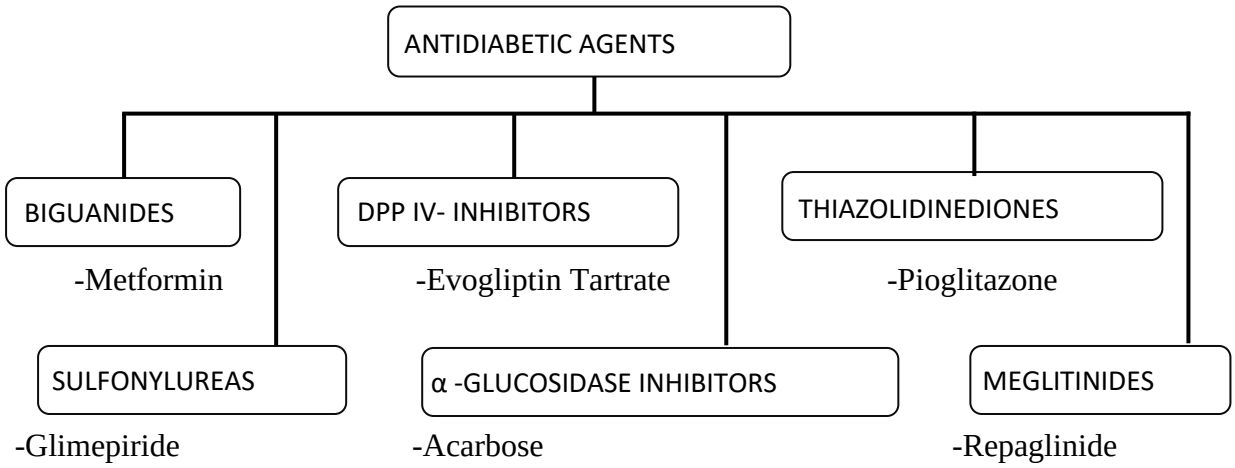

Figure 1: Classification of Anti diabetic drugs

2. INTRODUCTION OF METFORMIN HYDROCHLORIDE

BIGUANIDES

The history of biguanides began in the 19th century when it was found that the blood-glucose-lowering properties of the herb Galega officinalis (French lilac), used since the medieval age to treat polyuria and other diseases, were due to glargine, a derivative of guanidine contained in the plant seeds and flowers. The identification of glargine led to the synthesis of various biguanides (synthelin A and B, biguanide, metformin, phenformin, and

buformin) in the early 20th century that were tested as anti-diabetic agents but shortly discontinued due to toxicity issues or presumed low potency. [5]

♦ Mechanism of action

Metformin's mechanisms of action are unique from other classes of oral antihyperglycemic drugs. Metformin decreases blood glucose levels by decreasing hepatic glucose production (also called gluconeogenesis), decreasing the intestinal absorption of glucose, and increasing insulin sensitivity by increasing peripheral glucose uptake and utilization.[6] It is well established that metformin inhibits mitochondrial complex I activity, and it has since been generally postulated that its potent antidiabetic effects occur through this mechanism.[8] The above processes lead to a decrease in blood glucose, managing type II diabetes and exerting positive effects on glycemic control.

After ingestion, the organic cation transporter-1 (OCT1) is responsible for the uptake of metformin into hepatocytes (liver cells). As this drug is positively charged, it accumulates in cells and in the mitochondria because of the membrane potentials across the plasma membrane as well as the mitochondrial inner membrane. Metformin inhibits mitochondrial complex I, preventing the production of mitochondrial ATP leading to increased cytoplasmic ADP: ATP and AMP: ATP ratios (Fig. 2). [7] These changes activate AMP-activated protein kinas (AMPK), an enzyme that plays an important role in the regulation of glucose metabolism. [9] Aside from this mechanism, AMPK can be activated by a lysosomal mechanism involving other activators. Following this process increases in AMP: ATP ratio also inhibit fructose-1, 6-bisphosphatase enzyme, resulting in the inhibition of gluconeogenesis, while also inhibiting adenylate cyclase and decreasing the production of cyclic adenosine monophosphate (cAMP), [7] a derivative of ATP used for cell signaling. [10] Activated AMPK phosphorylates two isoforms of acetyl-CoA carboxylase enzyme, thereby inhibiting the fat synthesis and leading to fat oxidation, reducing hepatic lipid stores and increasing liver sensitivity to insulin. [7]

In the intestines, metformin increases anaerobic glucose metabolism in enterocytes (intestinal cells), leading to reduced net glucose uptake and increased delivery of lactate to the liver. Recent studies have also implicated the gut as a primary site of action of metformin and suggest that the liver may not be as important for metformin action in patients with type 2 diabetes. Some of the ways metformin may play a role in the intestines is by promoting the

metabolism of glucose by increasing glucagon-like peptide I (GLP-1) as well as increasing gut utilization of glucose. [7]

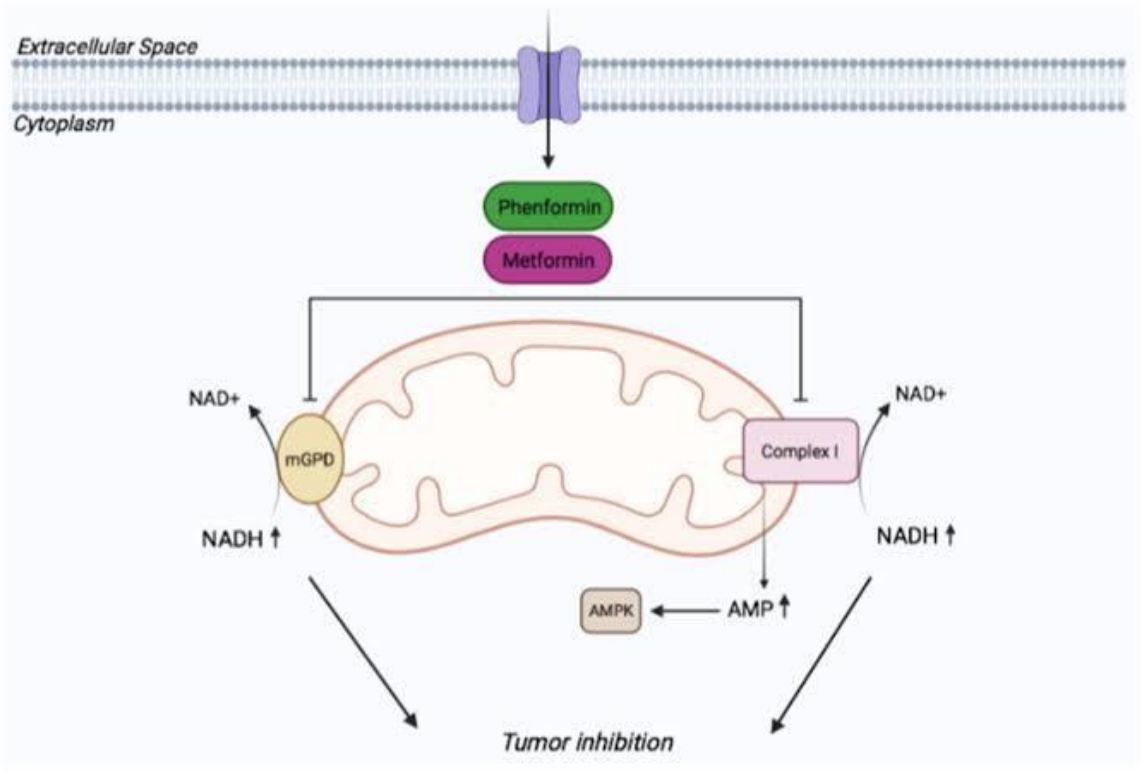

Figure 2: Mechanism of Action of Biguanides

METFORMIN HYDROCHLORIDE

Metformin is a biguanide antihyperglycemic agent and first-line pharmacotherapy used in the management of type II diabetes. [11]

Metformin was first approved in Canada in 1972 and received subsequent FDA approval in the US in 1995. [12]

♦ Pharmacokinetics of drug

Absorption:

Regular tablet absorption: The absolute bioavailability of a metformin 500 mg tablet administered in the fasting state is about 50%-60%. Single-dose clinical studies using oral doses of metformin 500 to 1500 mg and 850 to 2550 mg show that there is a lack of dose proportionality with an increase in metformin dose, attributed to decreased absorption rather

than changes in elimination. At usual clinical doses and dosing schedules of metformin, steady-state plasma concentrations of metformin are achieved within 24-48 hours and are normally measured at <1 µg/mL.[13]

Extended-release tablet absorption: After a single oral dose of metformin extended-release, Cmax is reached with a median value of 7 hours and a range of between 4 and 8 hours. Peak plasma levels are measured to be about 20% lower compared to the same dose of regular metformin, however, the extent of absorption of both forms (as measured by area under the curve - AUC), are similar. [6]

The volume of distribution:

The apparent volume of distribution (V/F) of metformin after one oral dose of metformin 850 mg averaged at 654 ± 358 L.

Metabolism:

Intravenous studies using a single dose of metformin in normal subjects show that metformin is excreted as an unchanged drug in the urine and does not undergo hepatic metabolism (no metabolites have been identified in humans) or biliary excretion.

Route of elimination:

This drug is substantially excreted by the kidney. Renal clearance of metformin is about 3.5 times higher than creatinine clearance, which shows that renal tubular secretion is the major route of metformin elimination. After oral administration, about 90% of absorbed metformin is eliminated by the kidneys within the first 24 hours post-ingestion.

Indication:

Metformin immediate-release formulations**:** Metformin is indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients≥10 years old with type 2 diabetes mellitus. [13]

Metformin extended-release tablet (XR)**:** The extended-release formulation of metformin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Safety in children has not been determined to this date. [6]

♦ Drug profile

Chemistry of Metformin hydrochloride is N, N-Dimethylimidodicarbonimidic diamide (Fig. 3). Its Chemical formula is $C_4H_{11}N_5$. It is a novel molecule with a molecular weight 165.62 g/mol. The Partition co-efficient (log p) is 0.062 while Dissociation Constant (pka) is 12.4. The appearance is a white to off white crystalline compound and the melting point is 223-242°C. It is freely soluble in water and slightly soluble in alcohol. A 500 mg dose is prescribed orally twice a day. [14]

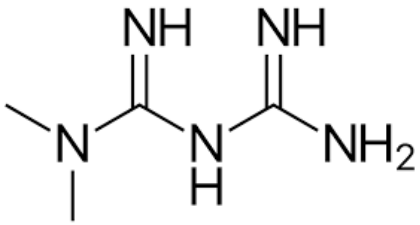

Figure 3: Structure of Metformin Hydrochloride

3. INTRODUCTION OF EVOGLIPTIN TARTRATE

DPP IV- INHIBITORS

Dipeptidyl peptidase-IV (DPP-IV) inhibitors are new class of oral diabetes drugs. Gliptins, also known as DPP-IV, are commonly used for patient with type-II diabetes who haven't reacted well to sulphonylureas and metformin. Dipeptidyl peptidase-IV inhibitors can help with weight loss and blood glucose control, but they've also been linked to an increased risk of pancreatitis.

They work by blocking the action of DPP-IV, an enzyme that destroys incretins (a group of gastrointestinal hormones). Incretins aids in the stimulation of insulin production when it is required (e.g., after eating) and the reduction of glucagon production by the liver when it is not required (e.g., during digestion).

They also decrease appetite & delay digestion. So, by defending incretins from damage, DPP-IV inhibitor helps to control blood glucose levels. [15] They do not cause hypoglycemia unless they are combined with other therapies that cause hypoglycemia. [17] After metformin and sulphonylureas, DPP-IV inhibitors can be used as a second or third-line treatment for patients with type-II diabetes, as a substitute to thiazolidinediones. [16]

Examples of DDP-IV inhibitors are Vildagliptin, Sitagliptin, Saxagliptin, Linagliptin, Gemigliptin, Anagliptin, Teneligliptin, Alogliptin, Trelagliptin, Omarigliptin, Evogliptin.

♦ Mechanism of action:

Evogliptin is a dipeptidyl peptidase IV inhibitor that is both competitive and reversible. This enzyme slows the breakdown of GLP-1(Glucagon-like peptide) and GIPs. GLP- 1 & GIP stimulates the release of insulin while inhibiting the release of glucagon from beta cell of pancreas (Fig. 4).[18] The repressive activity of Evogliptin compared to Sitagliptin is about 10- fold, also when compared to DPP8/9; Evogliptin has a 6,000 – fold higher selectively for DPP – IV. [19]

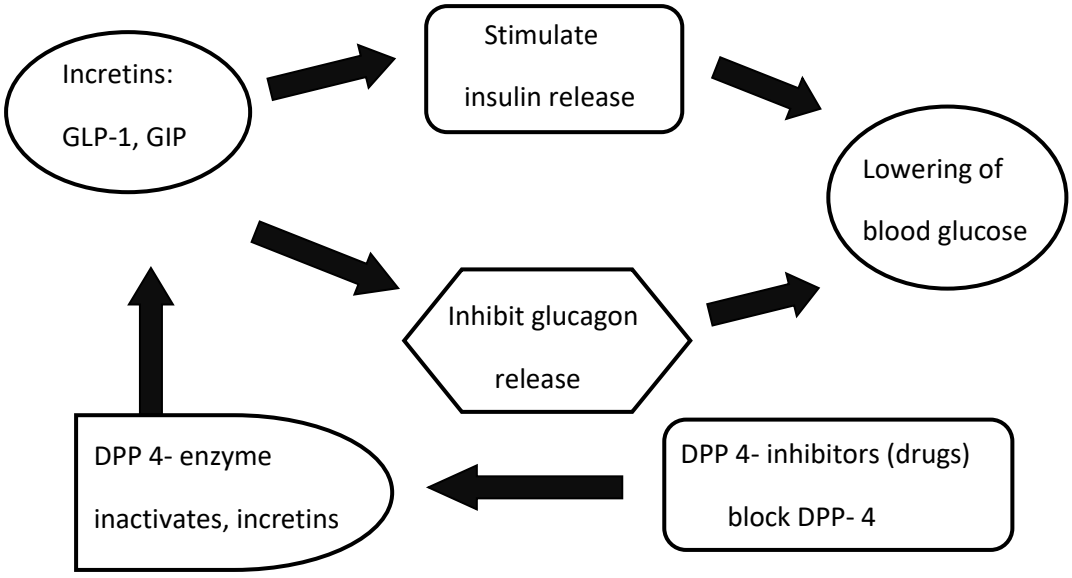

Figure 4: Mechanism of DPP-4 inhibitors.

EVOGLIPTIN TARTRATE

Evogliptin tartrate is a selective DPP-IV (dipeptidyl peptidase-4) inhibitor & it is prescribed in diabetes mellitus. It is also used as an anti-atherosclerosis drug when it targets arterial inflammation. [16]

Evogliptin is a β-amino amide derivative. [20] Dong-A ST which is a South Korean pharmaceutical company has developed Evogliptin. In South Korea, Evogliptin is approved for use. Evogliptin is derived from the words "Evo-lution" and "Gliptin," and it refers to an advanced type of gliptin that has the highest points of known DPP-IV inhibitors.

Evogliptin has a low risk of interaction with other co-administered medications, which can make it easier for patients to take several medications for chronic disease. [21]

♦ Pharmacokinetics of drug

Absorption:

The bioavailability of Evogliptin after unmarried oral control is extra than 50%. Concomitant control of Evogliptin with meals ingestion does not have an effect on the absorption. After single oral control of Evogliptin at dose of one.25–60 mg, time to acquire maximum recognition (t Cmax) among healthy sufferers emerge as three–5. Five hours. After single oral management of Evogliptin at the dose of five mg in wholesome volunteers, its most plasma consciousness (Cmax) turned into five.6 ± 1.3 μg/L. Dose boom results inside the boom of Cmax and the area beneath the curve "interest-time" (AUC_{last}). After multiple oral management of Evogliptin at doses of five mg, 10 mg, and 20 mg as quickly as each day, a regular state become reached via the zero.33 day of management. After accomplishing the steady state, Cmax of Evogliptin have become placed in four-5 hours after the drug management.

Distribution:

The distribution of Evogliptin between whole blood and plasma is almost the equal, about 46% of Evogliptin binds with plasma proteins. Non-clinical research set up that Evogliptin is quickly distributed in frame tissues (apart from heart tissue and mesentery). Evogliptin became detected within the blood flow of foetus, and it changed into excreted in milk of lactating rats.

Metabolism:

The most of Evogliptin circulating in the blood is the intact drug (greater than 80%). The biotransformation method consequences in five metabolites which have no DPP-4 inhibiting activity and are detected frequently in plasma and urine. Evogliptin is more regularly than now not metabolised with CYP3A4. In vitro research showed that Evogliptin did no longer inhibit CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 3A4 enzymes and did not result in CYP1A2, 2B6, 3A4 enzymes.

Excretion:

After unmarried management of Evogliptin at dose of 1.25–60 mg, the not unusual elimination half-life (t1/2) was from 32. Five to 39. Eight hours. After more than one management, the common removal half-life modified into from 32. Nine to 38.8 hours.

About 46.1% of the dose taken thru healthy person volunteers is excreted through urine and 42.8% of the dose is excreted thru faeces (which including metabolites).

Therapeutic Indication:

For the remedy of kind 2 diabetes mellitus as an accessory to weight loss plan and exercise to improve glycaemic manage, which used in combination with metformin.

Contraindication:

Evogliptin Tablets are contraindicated in patients with: Hypersensitivity to the drug or any of its component's severe ketosis, diabetic coma or pre-coma and kind 1 diabetes. [22]

♦ Drug profile

Chemistry of Evogliptin tartrate is (3R)-4-[(3R)-3-amino-4-(2, 4, 5-trifluorophenyl) butanoyl]-3-[(2-methylpropan-2-yl) oxymethyl] piperazin-2-one; (2R, 3R)-2, 3-dihydroxybutanedioic acid. [23] (Fig. 5) Its Chemical formula is $C_{23}H_{32}F_3N_3O_9$. Evogliptin is a hybrid peptide, which is a type of organic compound. These are compounds that contain at least two distinct groups of amino acids (alpha, beta, gamma & delta) connected by peptide bonds. [24] It is a novel molecule with molecular weight 551.5 g/mol. [25] The Partition co-efficient (log p) is 1.17 while Dissociation Constant (pka) is 13.69 (Strongest Acidic), -8.78 (Strongest basic). The appearance is white to off white solid and the melting point is 208-212°C. [26] It is easily soluble in water and slightly soluble in alcohol. A 5 mg dose is prescribed orally once a day.

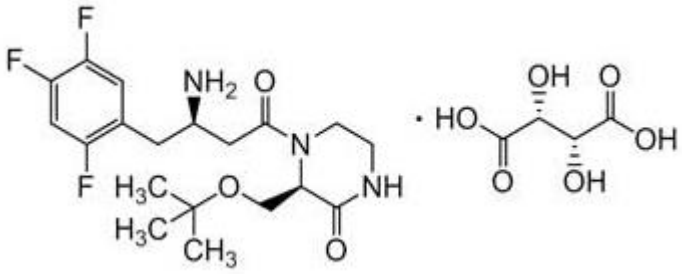

Figure 5: Structure of Evogliptin Tartrate

REVIEW OF LITERATURE

Table 1.1: Official methods for estimation of Metformin Hydrochloride

Sr. No.	Official In	Methods	Description	Ref. No.
1	Indian Pharmacopoeia 2018	Liquid Chromatography	**Stationary Phase:** A stainless steel column 30 cm x 4 mm, packed with octadecylsilane bonded to porous silica (10 µm) **Mobile Phase:** A solution containing 0.087% w/v of Sodium pentane sulphonate and 0.12% w/v of sodium chloride, adjusted to pH 3.5 using 1% v/v solution of orthophosphoric acid. **Flow rate:** 1 mL/min **Wavelength:** 218 nm **Injection volume:** 20 µL	27
2	British Pharmacopoeia 2003	Liquid Chromatography	**Stationary Phase:** Size = 0.25 m, Ø = 4.6 mm Stationary phase: irregular, porous silica gel to which benzene sulphonic acid groups have been chemically bonded (10 µm) Or Size = 0.11 m, Ø = 4.7 mm; Stationary phase: regular, porous silica gel to which benzene sulphonic acid groups have been chemically bonded (5 µm). **Mobile Phase:** 17 g/L solution of ammonium phosphate R adjusted to pH 3.0 with phosphoric acid R **Flow rate:** 1 mL/min **Wavelength:** 218 nm **Injection volume:** 20 µL	28

Table 1.2: Reported methods for estimation of Metformin Hydrochloride

<table>
<tr><th>Sr. No.</th><th>Method</th><th>Description</th><th>Ref. No.</th></tr>
<tr><td>1</td><td>Development and validation of UV Spectrophotometric method for estimation of Metformin in bulk and tablet dosage form.</td><td>Model: Shimadzu UV – 1800 240V
Solvent: Distilled water
Wavelength: 234 nm
Linearity: 10 – 50 µg/mL</td><td>29</td></tr>
<tr><td>2</td><td>Development and validation of UV Spectroscopic method for the determination of Metformin Hydrochloride in tablet dosage form.</td><td>Model: Shimadzu UV mini-1700
Solvent: 0.01N NaOH
Wavelength: 233 nm
Linearity: 1 – 25 µg/mL</td><td>30</td></tr>
<tr><td>3</td><td>Method development and validation of Metformin Hydrochloride in Tablet dosage form.</td><td>Model: Shimadzu UV 1700
Solvent: Methanol
Wavelength: 233 nm
Linearity: 8 – 13 µg/mL</td><td>31</td></tr>
<tr><td>4</td><td>Stability indicating UV spectroscopic method for the estimation of Metformin Hydrochloride in bulk and tablets.</td><td>Model: Shimadzu 1800
Solvent: Methanol
Wavelength: 232.2 nm
Linearity: 2 – 10 µg/mL
%Degradation:
<table>
<tr><th>Sr. No.</th><th>Condition</th><th>%Degradation</th></tr>
<tr><td>1</td><td>Acid</td><td>15.84</td></tr>
<tr><td>2</td><td>Alkali</td><td>18.94</td></tr>
<tr><td>3</td><td>Thermal</td><td>3.31</td></tr>
<tr><td>4</td><td>UV (254 nm)</td><td>9.51</td></tr>
<tr><td>5</td><td>UV (365 nm)</td><td>212.12</td></tr>
<tr><td>6</td><td>3% H_2O_2</td><td>22.14</td></tr>
</table></td><td>32</td></tr>
<tr><td>5</td><td>Method development and validation of forced degradation studies of Metformin Hydrochloride by using UV spectroscopy.</td><td>Model: Shimadzu 1700
Solvent: Methanol
Wavelength: 237 nm
Linearity: 1 – 10 µg/mL
%Degradation:
<table>
<tr><th>Sr. No.</th><th>Condition</th><th>Time</th><th>%Degradation</th></tr>
<tr><td rowspan="2">1</td><td rowspan="2">0.1N NaOH</td><td>60 min</td><td>8.07</td></tr>
<tr><td>90 min</td><td>11.95</td></tr>
<tr><td rowspan="2">2</td><td rowspan="2">3N HCl</td><td>60 min</td><td>9.75</td></tr>
<tr><td>90 min</td><td>12.79</td></tr>
<tr><td>3</td><td>30% H_2O_2</td><td>15 min</td><td>12.65</td></tr>
<tr><td>4</td><td>Dry Heat (70°C)</td><td>48 hrs</td><td>20.94</td></tr>
<tr><td>5</td><td>Photolytic</td><td>3 hrs</td><td>10.53</td></tr>
</table></td><td>33</td></tr>
<tr><td>6</td><td>Analytical method development and validation of Metformin Hydrochloride by</td><td>Stationary phase: Cosmosil C_{18} column (250mm × 4.6mm; 5µm)
Mobile Phase: Methanol: Phosphate buffer</td><td>34</td></tr>
</table>

	using RP – HPLC with ICH guidelines.	(pH- 3) (70:30 % v/v) **Flow rate:** 1 mL/min **Wavelength:** 238 nm **Linearity:** 10 - 50 µg/mL **Retention Time:** 4.2 min	
7	**RP-HPLC analytical method development and validation** OF **Metformin Hydrochloride** tablets assay	**Stationary Phase:** Hypersil ODS C_{18}, (250mm × 4.6mm; 5µm) **Mobile Phase:** Acetonitrile: Phosphate buffer (pH- 5.75) (65.35 % v/v) **Flow rate:** 1 mL/min **Wavelength:** 233 nm **Linearity:** 50 - 150 µg/mL **Retention Time:** 7.168 min	35
8	**Development and validation of an RP-HPLC method** for the determination of **Metformin Hydrochloride** in the pharmaceutical dosage form.	**Stationary Phase:** Zorbac- SCX C_{18}, (250mm × 4.6mm; 5µm) **Mobile Phase:** Ammonium-dihydrogen phosphate buffer (pH- 3): Acetonitrile (50:50 % v/v) **Flow rate:** 1 mL/min **Wavelength:** 218 nm **Linearity:** 20 - 60 µg/mL **Retention Time:** 11.12 min	36
9	**Simple and sensitive analytical method development and validation** of **Metformin Hydrochloride** by RP-HPLC.	**Stationary Phase:** Inertsil- Extend $C_{18,}$ (250mm × 4.6mm; 5µm) **Mobile Phase:** 1- Octane sulfonic acid: Acetonitrile (80:20 % v/v) **Flow rate:** 1 mL/min **Wavelength:** 232 nm **Linearity:** 1 - 250 µg/mL **Retention Time:** 10.78 min	37

Table 1.3: Reported method for estimation of Evogliptin Tartrate

Sr. No.	**Method**	**Description**	**Ref. No.**
1	**Development and validation of Novel UV Spectrophotometric method** for the determination of **Evogliptin Tartrate** in pharmaceutical dosage form1s.	**Solvent:** Deionized water **Wavelength:** 267 nm **Linearity:** 10 - 100 µg/mL	38
2	**Derivative Spectrophotometric method development and validation** for the estimation of **Evogliptin Tartrate** in the pharmaceutical dosage form.	**Solvent:** Deionized water **Wavelength:** 267 nm **Linearity:** 20 - 120 µg/mL	39
3	**Development and validation of RP-**	**Stationary Phase:** C_{18} (250 × 4.6	40

	HPLC method for estimation of **Evogliptin** in pharmaceutical dosage form.	mm; 5.0 µm) column **Mobile Phase:** Methanol: Water: Acetonitrile (70:20:10 % v/v/v) **Flow rate:** 1.0 mL/min **Wavelength:** 265 nm	
4	**Novel method development validation and stability-indicating assay method** for **Evogliptin tartrate** in pharmaceutical dosage form by RP-HPLC.	**Stationary Phase:** C_{18} (250 × 4.6 mm; 5.0 µm) column **Mobile Phase:** Methanol: Water: TFA mixture (70:30:0.1 % v/v/v) **Flow rate:** 1.0 mL/min **Wavelength:** 264 nm	41
5	**Development and validation stability indicating RP-HPLC method** for the estimation of **Evogliptin Tartrate** in pharmaceutical dosage form.	**Stationary Phase:** C_{18} (250 × 4.6 mm, 5.0 µm) column **Mobile Phase:** Buffer (pH 4.5): Methanol (45:55 % v/v) **Flow rate:** 1.0 mL/min **Wavelength:** 265 nm	42
6	Box–Behnken design-assisted optimization of **RP-HPLC** method for the estimation of **Evogliptin tartrate** by analytical quality by design	**Stationary Phase:** Water C_{18} (250 × 4.6 mm, 5.0 µm) column **Mobile Phase:** Buffer (pH 4.5): Methanol (60:40 % v/v) **Flow rate:** 1.0 mL/min **Wavelength:** 267 nm	43

Table 1.4: Reported methods for estimation of Evogliptin tartrate and Metformin hydrochloride.

Sr. No.	Method	Description	Ref. No.
1	**Development and validation of an RP-HPLC method** for the determination of **Metformin and Evogliptin** in bulk and pharmaceutical dosage forms	**Stationary Phase:** Column RP-18 (150 × 4.6 mm, 3.5µ) **Mobile Phase:** Acetonitrile: Phosphate buffer: Methanol (50:40:10% v/v/v) **Flow rate:** 1.0 mL/min **Wavelength:** 228 nm **Injection volume:** 10 µL **Retention Time:** 2.730 min	44

		(Metformin) and 4.468 min (Evogliptin tartrate)	
2	**Development and Analytical Method** Validation for Simultaneous Estimation of **Evogliptin Tartrate and Metformin Hydrochloride** in Combine Dosage Form	**Stationary Phase:** Column C_{18} **Mobile Phase:** Water: Acetonitrile (25:75 % v/v) **Flow rate:** 1.2 mL/min **Wavelength:** 210 and 230 nm **Retention Time:** 2.009 (Metformin) and 2.956 minutes (Evogliptin tartrate)	45
3	**RP-HPLC Based Stability Indicating Assay** of **Evogliptin and Metformin:** Development and Validation of the Analytical Method	**Stationary Phase:** C_{18} (4.6 × 150mm, 5µ Kromasil) column **Mobile Phase:** Phosphate buffer (pH 4.5) : Acetonitrile (30:70 % v/v) **Flow rate:** 0.8 mL/min **Linearity:** 10-50 µg/mL **Retention Time:** 7.03 min (Evogliptin tartrate) and 9.50 min (Metformin)	46

CONCLUSION

This review carried out an overview of Metformin Hydrochloric and Evogliptin tartrate. Metformin hydrochloric is a Bigunides that is used in diabetes mellitus. It is also used in pre-diabetes, PCOS, Gestational diabetes, Cancer. It increases the sensitivity of insulin by fat metabolism. Evogliptin tartrate is a DPP-IV inhibitor which is used in diabetes mellitus. It is also used as an anti-atherosclerosis drug when it targets arterial inflammation. DPP4 inhibitors (DPP41) are a modern class of diabetes medications that retain incretin hormones while increasing postprandial insulin secretion.

A simple and accurate UV, RP-HPLC and stability-indicating method was developed for estimation of Metformin hydrochloride and Evogliptin tartrate in pharmaceutical dosage form. The above method was evaluated for linearity, accuracy, precision, and robustness as per ICH guideline from this review study, it is possible to develop a new sensitive and accurate analytical method for anti-diabetic drug.

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