ABSTRACT

Obtaining the target blood glucose level by monotherapy can be challenging, especially for the patients who are suffering from other disease meanwhile. Polypharmacy is often required to achieve good metabolic control. Reducing treatment complexity can be achieved through the use of single-tablet fixed-dose combinations of two oral hypoglycemic agents. FDCs improve patient compliance by reducing the number of pills. A range of fixed dose combination oral hypoglycemic agents in several different dosage strengths are available. Clinical studies revealed that fixed-dose combinations had many benefits compared to single entity and separate agents in terms of effects, convenience, compliance, and cost. Present article includes advantages, regulatory status, criteria and risk factors for use of FDC for the type 2 diabetes mellitus treatment.

KEY WORDS: Fixed Dose Combination, Therapeutic potential, Diabetes mellitus.

1. INTRODUCTION

Fixed dose combination (FDC’s) products, with two or more drugs co-formulated in one dosage form having corresponding mechanism of action and increased therapeutic activity showing new possibilities in the treatment of almost every human disease. The development of FDC’s is becoming increasingly important from a public health viewpoint. FDC’s has improved therapeutic activity, simplified treatment procedure, enhanced patient compliance and more cost-effective dosage formulations. The advancement of FDC’s product is
especially to promote patient compliance, reduced side effects and superior therapeutic value of active drug together.

FDC’s product
“FDC is combination of two or more active pharmaceutical ingredient of fixed ratios combined in a single dosage form.\(^1\)

World Health organization (WHO) definition
A combination of two or more actives in a fixed ratio of doses. This term is used generically to mean a particular combination of actives irrespective of the formulation or brand. It may be administered as single entity products given concurrently or as a finished pharmaceutical product.\(^2\)

FDC’s is frequently used in cure of almost every disease specially diabetes mellitus, tuberculosis, malaria, AIDS & hypertension etc. FDC’s must be based on convincing therapeutic rationalization and be carefully justified and clinically significant.\(^3\) FDC’s preferably offer synergistic effect of two or more API with reduced side effects. FDC’s drug products are mainly used to reduce numbers of pill burden and to optimize the therapy of various diseases. FDC’s offers increased bioavailability of anti-diabetic drugs in relevant to their simultaneous administration as separated pills, thus reduced the number of pills to take at a time.\(^4\) It is cheaper to acquire a FDC’s product than to acquire single product individually. This article examines the use of FDC’s verses separate pills combination therapy with same drug for the treatment of diabetic mellitus and it gives ideas to prescribers, payers and patients.\(^5\)

2. ADVANTAGES OF FIXED-DOSE COMBINATIONS

2.1 Mono-therapy versus combination therapy
Applied combination therapy for the treatment of T2DM with oral hypoglycemic agent with reduced numbers of daily tablets or doses or other co-medications shows good adherence of patient. Combination products make particular intelligence in the treatment of contagious disease, where partial adherence can lead to the development of drug-resistant strains and a threat to public health. Reduce difficulty of a dosage regimen due to lesser number of medications at a time will also enhance patient compliance.
2.2 Combination therapy with separate agents versus fixed-dose combinations

Combination therapy where classified in two methods: one is various drugs where prescribed separately and the other is FDC. Combination therapy with separate agents rises as substitute for the patients who fail in maintaining blood sugar level by mono-therapy. Separate agents prescribed in various number of pills give rise in complication by increased numbers of medication at a time such type of problem can be easily solve by prescribing FDC which offers simple regimen with less pills or once-daily dosing.\cite{6}

2.3 Fixed Dose Combination

Reducing the number of medication diminishes the complexity of the regimen, so that superior patient adherence is anticipated with combination products. In diabetic mellitus treatment, combination rationales for the most commonly employed FDC products are to provide rationale drug regulatory mechanism and enhance drug therapeutic effectiveness. Numbers of fixed dosed FDC products are commercially available with corresponding mechanism of action to enhance glycemic control in the type 2 diabetes patients. Example: Pioglitazone and glimepiride, etc. Procurement, management and handling of drugs are simplified with the use of fixed dose combinations. Combination therapy of antidiabetic agents with different mechanisms of action maintains greater glycemic control at lower doses than a high dose of 1 agent while causing fewer side effects.\cite{7} The below figure 1 demonstrate the advantages of FDC over separate or monotherapy.

![Figure 1: Demonstrate the advantages of FDC over separate or monotherapy.](image-url)
3. REGULATION OF FDC PRODUCTS

As per the Drugs and Cosmetic Act, 1940, any new drug and the authorization to market a drug is to be given by the DCGI. Before the approval of any drug, the Central Drugs Standard Control Organization (CDSCO) undergoes a process with respect to their quality, safety and efficacy. It is an accepted fact that FDC’s is treated as a new drug, for the reason that by combining two or more drugs, the safety, efficacy, and bioavailability of the individual active pharmaceutical ingredient may change. The DCGI monitors the drug formulations, including the combinations of drugs, from the angle of safety, effectiveness and rationality. Globally, there is a rising movement to license FDC’s products for the marketplace. Appendix VI of Schedule Y (Drugs & Cosmetics Rules 1945) specifies the necessities for authorization for marketing of a variety of types of FDC’s. FDA guidelines apply to manufacture / import and marketing approval of FDC’s as a complete pharmaceutical product considered as new drug as per Rule 122(E) of Drugs and Cosmetics Act & Rules. A clear explanation with an appropriate therapeutic rationale of the particular combination of active substances proposed will be the basis of approval. It is not always necessary to generate new information. Confirmation may be obtained from the scientific literature, subject to its being of sufficient value. In case of FDC’s where all the active ingredients are approved individually, if a clinical trial (CT) is necessary, confirmatory study to establish efficacy, preferably by similar group comparisons in which the FDC’s is compared to its individual substances may be considered. When possible, a placebo arm may be incorporated. Comparative CT’s of the FDC’s with reference treatment may be essential, particularly when the therapeutic explanation talks more on the FDC’s superiority over a reference treatment. An application for a marketing authorization may comprise entirely original data, entirely data from the literature and both original data and data from the literature (“hybrid”). For FDC’s, it is likely that hybrid submissions will be the most ordinary kind. Chemical and pharmaceutical data should be always completely innovative, unless there is enough explanation with literature when partial data can be in-original. Treasury Challan: of INR 15,000 if all active ingredients are approved in India for more than one year, or INR 50,000 in case any of the active ingredients is unapproved or approved for less than one year. However, a Challan of only INR 15,000 is required, in case the applicant has already submitted an application along with a Challan of INR 50,000 towards any of the single active ingredient approval, which is less than 1 year old. Any test batch/trial batch of new drugs for test and analysis purpose should be manufactured after obtaining License in Form 29 from the concerned State Licensing...
Authority and copy of the license should be submitted along with the application for seeking permission to manufacture and market the new drug.\textsuperscript{[1, 8]}

4. **FDC FOR DIABETICS MELLITUS**

Type 2 diabetes mellitus (T2DM) is a chronic, progressive disorder managed using long-term oral antihyperglycemic agents (OHAs). Treatment adherence to OHA’s is important for maintaining glycemic control. In T2DM an insulin sensitizer (metformin or a thiazolidone [TZD]) may be usually combined with insulin secretagouge (a sulfonylurea or a meglitidine) or an insulin-based agent (a glucagon-like peptide-1 [GLP-1] receptor agonist or a dipeptidyl peptidase-4 [DPP-4] inhibitor). Impaired insulin secretion results for the most part from progressive beta-cell dysfunction and loss of beta-cell mass. Elevated hepatic gluconeogenesis is developed due to insulin resistance in liver and also in muscle and fat. Deficiency in GLP-1 due to incretin impairment in T2DM and also result in decreased sensitivity to the insulin-simulatory effects of both GLP-1 and glucose dependent insulin tropic polypeptide (GIP).\textsuperscript{[9]} Increased risk of diabetic complications due to monotherapy to target a single defect is often inadequate to achieve glycemic goals. Consequently use of FDC’s with complementary mechanism of action has become keystone of T2DM management.\textsuperscript{[10]}

Considerable interest emerging in the use of FDC’s single-tablet combination of oral anti-diabetic agents in long term therapy. These can conveniently reduce the numbers of daily medication taken by diabetic patient and may potentially improve adherence. Metformin is generally preferred as initial pharmacological therapy for T2DM and many of the presently available FDC’s of oral anti-diabetic agents have incorporated metformin along with other anti-diabetic agents as shown below in table 1.\textsuperscript{[11]} The association of the patients towards the combinational therapy is much needed to take all advantage form it. The worldwide prevalence of diabetes mellitus was 246 million in 2007 and is expected to increase to 380 million by 2025 and it accounts for 85% to 95% of cases. In a retrospective, observational study, 59 patients with type 2 diabetes who had been receiving concurrent treatment with glyburide + metformin administered separately were administered an FDC tablet of glyburide (glibenclamide)/metformin or continued to receive each drug separately. Combination of a sulfonylurea + metformin is among the OHAs that might be prescribed. This apparent additive effectiveness might be explained by the complementary mechanisms of antihyperglycemic action of the 2 drugs (i.e., the stimulated insulin secretion of pancreatic β
cell by the sulfonylurea and the enhanced insulin sensitivity of the hepatic and peripheral tissues by metformin). The sulfonylurea glimepiride might offer some advantages as a component for an FDC’s with metformin due to its more outstanding extra pancreatic activity and more favorable safety profile compared with those of other sulfonylureas.\textsuperscript{[12]} Retrospective observational studies from large database and smaller prospective specific OHA studies suggest that >80 or 90% satisfactory adherence of patients towards combinational therapy. In patients with T2DM inadequately controlled on metformin alone (>1500 mg/day), saxagliptin 5 mg added to metformin provided sustained clinically meaningful glycemic improvements (reductions in HbA1c, fasting plasma glucose (FPG) and postprandial plasma glucose (PPG) levels) after 24 weeks, which were sustained over 102 weeks. Combination therapy was generally well-tolerated with no increase in hypoglycemia or body weight. saxagliptin + metformin as initial therapy lead to statistically significant improvements compared with either treatment alone across key glycemic parameters (HbA1c, FPG, PPG) with a tolerability profile similar to the monotherapy components and no increase in hypoglycemic episodes.\textsuperscript{[5]} Saxagliptin 2.5 mg/day was shown to offer sustained efficacy and good tolerability for patients with T2DM and moderate to severe RI, both after 12 weeks and after 52 weeks. Interestingly, it was also suggested that metformin can be used in such patients with mild to moderate RI provided that the dose is reduced (e.g., by 50% or to half-maximal dose) and that careful monitoring of renal function is done.
Table 1: List of some presently available FDC of anti-diabetic agents has incorporated metformin along with other antidiabetic agents.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Name Of Drug</th>
<th>Indication</th>
<th>Date of approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Gliclazide 40mg/80mg + MetFormin Hcl 500mg + Rosiglitazone 2mg tablet</td>
<td>Ant-diabetic</td>
<td>22.08.2006</td>
</tr>
<tr>
<td>2.</td>
<td>Pioglitazone 15mg/30mg + Metformin ER 1000mg tablet (additional strength)</td>
<td>For second line therapy in type-II diabetes</td>
<td>23.01.2007</td>
</tr>
<tr>
<td>3.</td>
<td>Rosiglitazone 1mg + Metformin HCl 500mg tablet (additional strength)</td>
<td>Patients with type 2 diabetes mellitus when dist exercise and the single agent do not result Rosiglitazone 2mg in adequate glycemic control</td>
<td>08.02.2007</td>
</tr>
<tr>
<td>4.</td>
<td>Glibenclamide 5mg + Metformin SR 850mg tablet (additional strength)</td>
<td>non insulin dependent diabetes mellitus patients poorly controlled with sulphonylurens or biguanide alone</td>
<td>15.02.07</td>
</tr>
<tr>
<td>5.</td>
<td>Glimepiride 1mg/2mg. + Metformin SR 1000mg tablet (additional strength)</td>
<td>For patients with type diabetes mellitus when diet exercise &amp; the agent do not result in adequate glycemic control.</td>
<td>08.06.2007</td>
</tr>
<tr>
<td>6.</td>
<td>Miglitol (50mg) + Metformin HCl SR (500mg) tablet.</td>
<td>For adult with Type-II diabetes mellitus where simple drug therapy, diet and exercise do not result in adequate glycemic control.</td>
<td>31.10.2007</td>
</tr>
<tr>
<td>7.</td>
<td>Vildagliptin 50/50/50mg + Metformin 500/850/1000mg Tablet</td>
<td>For the treatment of Type II diabetes mellitus when single drug therapy along with diet, exercise do not result in adequate glycemic control</td>
<td>21.07.2008</td>
</tr>
<tr>
<td>8.</td>
<td>Metformin HCl ER 500mg + Fenofibrate 80mg/160mg tablet</td>
<td>For the treatment of Type-II diabetes associated with mixed dyslipidemia</td>
<td>25.01.2008</td>
</tr>
<tr>
<td>9.</td>
<td>Sitagliptin (As Phosphate) 50mg + Metformin HCl. 500mg/1000mg Film coated tablets</td>
<td>As an adjunct to diet &amp; exercise to improve glycemic control in patients with type-two diabetes mellitus</td>
<td>28.04.2008</td>
</tr>
<tr>
<td>10.</td>
<td>Vildagliptin 50mg/50mg/50mg + Metformin Hcl 500mg +850mg +1000mg tablets</td>
<td>For the treatment of type 2 diabetes mellitus when single drug therapy along with diet, exercise do not result in adequate glycemic control</td>
<td>21.07.2008</td>
</tr>
<tr>
<td>11.</td>
<td>Glibenclamide 5mg + Pioglitazone 15mg + Metformin500mg film coated tablets</td>
<td>As 3rd line treatment of type II diabetes mellitus when diet, exercise and the single agents and the second line therapy with two drugs do not result in adequate glycemic control</td>
<td>23.02.2009</td>
</tr>
<tr>
<td>12.</td>
<td>Voglibose 0.2 mg + Metformin 500mg Tablets</td>
<td>As 2nd line treatment of type II Diabetes mellitus when diet, exercise and the single agent do not result in adequate glycemic control.</td>
<td>13.07.2009</td>
</tr>
<tr>
<td>13.</td>
<td>Glimepiride 1/2 mg + Metformin 500 mg + Atorvastatin 10 mg tablets</td>
<td>For the treatment of type II diabetes mellitus associated with dyslipidemia</td>
<td>17.12.2009</td>
</tr>
<tr>
<td>14.</td>
<td>Metformin HCl 850mg + Sitagliptin Phosphate 50mg Tablet</td>
<td>As an adjunct to diet &amp; exercise to improve glycemic control in patients with type-two diabetes mellitus</td>
<td>15.12.2009</td>
</tr>
<tr>
<td>No.</td>
<td>Drug Name</td>
<td>Details</td>
<td>Date</td>
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</tr>
<tr>
<td>15</td>
<td>Acarbose 25mg/50mg + Metformin 500mg/500mg FC Tablet</td>
<td>For the treatment of patients with Type II diabetes mellitus, when diet, exercise and single agent does not result in adequate glycemic control.</td>
<td>23.02.2009</td>
</tr>
<tr>
<td>16</td>
<td>Miglitol 25 mg + Metformin 500mg tablets</td>
<td>For adult with Type-II diabetes mellitus where simple drug therapy, diet and exercise do not result in adequate glycemic control.</td>
<td>16.03.2010</td>
</tr>
<tr>
<td>17</td>
<td>Metformin SR 500mg/500mg + GliclazideSR 60mg/30mg + Pioglitazone 15mg/15mg tablets</td>
<td>As 3rd line treatment of type II diabetes mellitus when diet, exercise and the single agents and the second line therapy with two drugs do not result in adequate glycemic control</td>
<td>28.05.2010</td>
</tr>
<tr>
<td>18</td>
<td>Gliclazide 40/80mg+Metformin 500mg+Pioglitazone15mg Tablet</td>
<td>As 3rd line treatment of type II diabetes mellitus when diet, exercise and the single agents and the second line therapy with two drugs do not result in adequate glycemic control</td>
<td>19.07.2010</td>
</tr>
<tr>
<td>19</td>
<td>Voglibose 0.3mg + Metformin (SR) 500mg Tablet</td>
<td>As 2nd line treatment of type II Diabetes mellitus when diet, exercise and the single agent do not result in adequate glycemic control.</td>
<td>08.06.2010</td>
</tr>
<tr>
<td>20</td>
<td>Metformin 500/500mg + Repaglinide 1/2mg Tablet</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are already treated with a meglitinide &amp; metformin or who have inadequate glycemic control on a meglitinide alone or metformin</td>
<td>20.08.2010</td>
</tr>
<tr>
<td>21</td>
<td>Metformin (ER )1000mg/500mg +Saxagliptin 2.5 mg/5mg Tablets</td>
<td>As an Adjunct to diet and exercise to improve glycemic control in adults patients with type 2 diabetes mellitus when treatment with both Saxagliptin and Metformin is appropriate</td>
<td>19.09.2011</td>
</tr>
<tr>
<td>22</td>
<td>Linagliptin 2.5mg/2.5mg/2.5mg + Metformin 500mg/850mg/1000mg Film coated Tablets</td>
<td>As an adjunct to diet and exercise to improve glycemia control in adults with type II Diabetes Mellitus when treatment with Linagliptin and Metformin is appropriate</td>
<td>26.07.2013</td>
</tr>
<tr>
<td>23</td>
<td>MetforminHCl500mg/850mg/1000mg+Vildagliptin50mg/50mg/50mg Film coated Tablet ( additional indication)</td>
<td>For the treatment of Type 2 Diabetes mellitus having HbA1c &gt; 8% where diabetes is not adequately controlled by diet and exercise alone.</td>
<td>22.10.2013</td>
</tr>
<tr>
<td>24</td>
<td>Glimepiride IP 0.5 mg+ Metformin Hydrochloride ER 500 mg uncoated bilayered tablets(additional strength)</td>
<td>As an adjunct to diet and exercise in type 2 diabetes mellitus patients, when monotherapy is not able to achieve glycemic control.</td>
<td>20.01.2014</td>
</tr>
</tbody>
</table>
In the US, the approved use of metformin extended-release + saxagliptin is as adjunct to diet and exercise in T2DM when treatment with both saxagliptin and metformin is appropriate. Saxagliptin is indicated in adult patients aged 18 years and older with T2DM to improve glycemic control in combination with metformin, when metformin alone, with diet and exercise, does not provide adequate glycemic control. Saxagliptin in combination with metformin is an efficient, safe and tolerable combination therapy for T2DM and the new saxagliptin-metformin FDC’s offer some advantages for clinical use.\textsuperscript{[13]} Frequently used monotherapies mainly includes metformin and sulfonylureas have been associated with a loss of glycemic control and a decline in beta-cell function. A randomized, controlled clinical study demonstrated that combination therapy with pioglitazone and a sulfonylurea produced significantly greater improvements in glycosylated hemoglobin A1C and fasting plasma glucose than those observed for sulfonylurea monotherapy.\textsuperscript{[14]} Two dosage strengths of a fixed-dose combination (FDC) tablet containing 30 mg of pioglitazone and either 2 or 4 mg of glimapiride have been developed as a once-daily treatment for T2DM in patients who require combination oral therapy. The pioglitazone + glimapiride FDC product offers the convenience of a single-tablet product when multiple oral therapies are needed to achieve and maintain glycemic control.\textsuperscript{[15]} T2DM patients inadequately controlled on pioglitazone (30 to 45 mg/day) with addition of sitagliptin (100 mg/day) will reduce HbA1c over 24 weeks by 0.70%. Considerable reductions in hyperglycemia were associated with no significant change in fasting plasma insulin, but there were marginal reductions in fasting pro-insulin and the pro-insulin/insulin ratio. Insulin resistance did not appear to be significantly changed and reductions in fasting and postprandial glucose were also observed with continues use of FDC’s.\textsuperscript{[10]} Use of combinations of those drugs that do not cause hypoglycemia (metformin, thiazolidinediones, DPP4 inhibitors, α-glucosidase inhibitors), at an early stage of the disease to achieve therapeutic hemoglobin A1c (HbA1c) levels (below 6.5%) has also been advocated. Compliance is improved and cost lowered when multiple drugs are provided in a single tablet or capsule, and FDC’s of two oral hypoglycemic agents have been available for many years.\textsuperscript{[16]} Metformin, which suppresses hepatic gluconeogenesis, is usually accepted as a first-line pharmacologic therapy for handling of hyperglycemia .\textsuperscript{[10]} Benefits of metformin include demonstrated glycaemic efficacy, weight loss and a potential benefit on mortality in overweight patients.\textsuperscript{[17]}
5. CRITERIA FOR THE USE OF FDC IN THE TREATMENT OF T2DM

5.1 Tolerability

Tolerability is equivalent with combination therapy delivered as an FDC’s or as individual pills because the dosage is regularly similar with both regimens. The perceptions that it is difficult to attributes adverse effects to particular components of a FDC’s may be valid in the case if initial combination therapy in a drug-native patient, but that concern would also apply to dual therapy.\[18\] For patients who have switched from monotherapy to dual therapy to a comparable regimen delivered via an FDC’s would not be expected to cause new tolerability issues. Relatively few published articles have assessed whether FDC’s formulations provide better glycemic control than separate medication therapy.\[19\]

5.2 Dosing Flexibility

The currently available FDC’s for use in patients with T2DM are formulated in a variety of useful dosage combinations, as shown in Table 1. It should be kept in mind that dosing flexibility with individually administered drug is limited to combinations reflecting the available formulations of each drug.\[9\]

5.3 Adherence

Approximately 50% of patients with chronic diseases show poorer-than-expected responses to prescribed medication because of inadequate adherence, a problem that applies to patients with T2DM. In a chronic complex conditions in which polypharmacy are common, a reduction in pill burden could potentially enhance adherence, which may be achieved with FDC’s.\[20\] In a retrospective analysis of outcomes among more than 11,000 diabetic patients in a managed-care organizations, non-adherence to oral antihyperglycemic medications (administered in <80% of the total number of days covered by filled prescriptions) was associated with statically significant increase in all-cause mortality and all cause hospitalization; conversely, each 25% increase in adherence to antihyperglycemic medication was associated with a 0.05% decrease (95% CI, -0.08 to -0.01) in A1C. Similarly, analyses of pharmacy claims for patients with T2DM have reveled that a 10% poorer score on an adherence measure corresponds with a 0.14% increase in A1C. Among patients with T2DM using combination therapy, adherence tends to be greater with FDC’s than with separate pills and greater after switching from monotheary to an FDC rather than to separate pills combinations.
5.4 Cost Effectiveness
Inadequate adherence to treatment for diabetes was linked to more healthcare utilization and higher costs (although the review also revealed wide methodological variability among cost-effectiveness studies). FDC’s for T2DM can smooth the progress of adherence and thereby reduce the lasting risk of complications and emergencies requiring hospitalization, they have the potential to reduce overall expenditures for patients with T2DM.

6. Risk factors for type 2 diabetes
Patients with T2DM have a significantly greater risk of cardiovascular disease, including coronary heart disease, stroke, and peripheral vascular disease, in addition to the well-known micro vascular complications such as retinopathy, neuropathy, and nephropathy. Studies have shown that micro vascular complications can be reduced by intensive glycemic control in both type 1 and type 2 diabetes mellitus. Cardiovascular risk associated with T2DM comprises a cluster of comorbidities, including abdominal obesity, insulin resistance, hypertension, and dyslipidemia. Patients with T2DM also have confirmation of low-grade systemic inflammation, with increased levels of inflammatory markers such as high-sensitivity C-reactive protein and decreased levels of the anti-inflammatory molecule adiponectin. Adiponectin is the most abundant protein released from adipocytes into the circulation, and reduced adiponectin is linked with the components of the metabolic syndrome, such as increased insulin resistance and blood glucose, decreased fatty acid metabolism, elevated TGs, and reduced HDLC. Adiponectin also has anti-inflammatory effects, and its gene expression can be activated by peroxisome proliferator-activated receptor gamma agonists. The high risk of CVD in patients with T2DM that the combination of pioglitazone and metformin in an FDC resulted in similar or improved beneficial effects on circulating biomarkers of CVD compared with each monotherapy. In patients with diabetes, hyperglycemia induces superoxide overproduction, which is accompanied by an increase in nitric oxide generation. The increase in oxidative and nitrosative stress ultimately activates poly (adenosine diphosphate-ribose) polymerase, which subsequently ribosylates glyceraldehyde-3-phosphate dehydrogenase, leading to acute endothelium dysfunction that contributes to diabetic complications. It is well established that patients with diabetes early intensive to achieve glycemic goals can significantly reduce the risk for vascular complications and potentially preserve beta-cell function. Recent interest in preventing incident diabetes has focused on those patients with impaired glucose metabolism. There is a
twofold greater risk of developing diabetes in hypertensive patients compared with normotensive patients.[24]

7. CONCLUSION
Type 2 diabetes mellitus have been identified a chronic disease with increase numbers of patients day by day worldwide. Treatment therapy developed with the use of combination of drugs with increase efficasy, well tolerability, dosing flexibility, increase patients adherence and cost effective dosage formulation with minimum side effects. The purpose of this review work is to address any false perception on the physicians, patients or buyers that may affect utilization of FDC’s for the treatment of T2DM. Based on the review done, it is noticeable that FDC offers several advantages over the monotherapy. Additionally FDC also increase patient’s adherence towards treatment therapy. Availability of FDC in different dosage strength formulations allows for flexibility in selection and adjustment of dosage. FDC formulations may provide an opportunity to improve care. FDC offers an efficient, safe and tolerable treatment therapy for T2DM. From the review it is reveled that long- term treatment therapy for T2DM suitable with the use of FDCs over monotherapy.

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