REVIEW ARTICLE

SMART-DM: Simplified Diabetes Management for Primary Care Physicians

ANUJ MAHESHWARI*, MANGESH TIWASKAR†, RAJDEEP SAHA‡, AJAY BUDHWAR#, KAMAL KUMAR¥, SHILPA CHOUDHARY§

ABSTRACT

Type 2 diabetes mellitus (T2DM) is a progressive metabolic disorder characterized by insulin resistance and declining beta-cell function, often leading to chronic hyperglycemia and associated complications. Despite the availability of various pharmacological agents, glycemic control remains suboptimal in a significant proportion of patients, particularly when relying solely on monotherapy or delayed combination strategies. This review explores the current challenges in diabetes management within primary care settings, highlighting the limitations of monotherapy and dual therapy approaches. It emphasizes the role of early, individualized treatment intensification using triple combination therapy involving metformin, dapagliflozin, and sitagliptin. This combination targets complementary pathophysiological pathways - hepatic glucose production, renal glucose reabsorption, and incretin hormone regulation - offering superior glycemic control, reduced risk of hypoglycemia, weight management, and cardiorenal benefits. The SMART-DM framework is introduced as a simplified and actionable approach to guide physicians in optimizing diabetes care. In alignment with global and national clinical guidelines, this review supports the timely adoption of fixed-dose triple therapy to overcome clinical inertia and improve treatment adherence. Additionally, the review discusses evidence from key clinical trials, patient selection considerations, and safety profiles, thereby providing a comprehensive guide for health care practitioners aiming to enhance long-term outcomes in patients with T2DM.

Keywords: Type 2 diabetes mellitus, triple combination therapy, metformin, dapagliflozin, sitagliptin, fixed-dose combination, SMART-DM

Diabetes mellitus is a long-term metabolic condition marked by elevated blood glucose levels, primarily due to inadequate insulin secretion or the inability of the body to utilize insulin efficiently[1]. Data from the International Diabetes Federation (IDF) Diabetes Atlas 2025 showed that 589 million individuals aged between 20 and 79 years are currently living with diabetes globally. This number is expected to surge to 853 million by the year 2050, highlighting its rapidly growing prevalence[1].

The condition poses a significant public health challenge worldwide, largely due to its link with severe complications such as cardiovascular diseases (CVDs), nerve damage, kidney dysfunction, and vision impairment[2]. In India, the diabetes burden is escalating alarmingly from an estimated 77 million adults in 2019 to a projected 134 million by 2045[3].

Diabetes mellitus is generally categorized into two primary types: Type 1 and type 2 (Fig. 1). Type 1 diabetes is an autoimmune disorder in which the immune system targets and destroys the insulin-producing beta-cells of the pancreas, leading to an absolute deficiency of insulin[4].

In contrast, type 2 diabetes mellitus (T2DM) develops due to the reduced sensitivity of the body to insulin combined with an inadequate compensatory insulin response. This form of diabetes is frequently associated with factors such as excess body weight, lack of physical activity, and inherited genetic predisposition. It accounts for 90%-95% of cases globally[2]. T2DM is a growing global health concern driven by aging, urbanization, and

*Professor in Medicine, Hind Institute of Medical Sciences, Ataria, Sitapur, Uttar Pradesh, India
†Consultant Physician and Diabetologist, Shilpa Medical Research Centre, Mumbai, Maharashtra, India
‡Consultant Physician, Chakraborty Medical-1, Kolkata, West Bengal, India
#Consultant Physician, Budhwar Diabetes Clinic, Amritsar, Punjab, India
¥Deputy General Manager
§Medical Affairs Manager
Medical Services Dept., Alembic Pharmaceuticals Ltd., Andheri East, Mumbai, Maharashtra, India
Address for correspondence
Dr Kamal Kumar
Deputy General Manager
Medical Services Dept.
Alembic Pharmaceuticals Ltd.
2nd Floor, Prime Corporate Park, Behind ITC Grand Maratha Sheraton, Sahar Road, Andheri East - 400 099, Mumbai, Maharashtra, India
E-mail: kamal.kumar@alembic.co.in

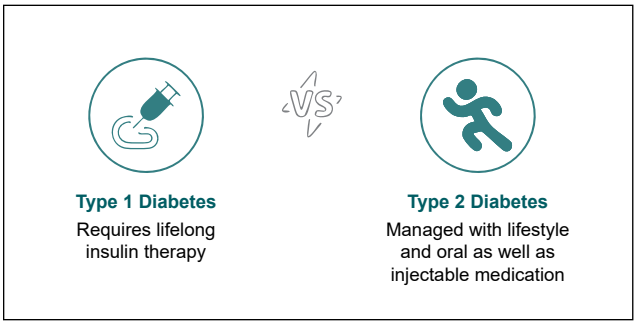


Figure 1. Broad classification of diabetes mellitus.

lifestyle changes. It develops gradually and may go undiagnosed, increasing the risk of complications associated with hyperglycemia[4]. Early detection and management through lifestyle changes and medication are essential to reduce morbidity and mortality[5].

Diabetes management is inherently complex, requiring sustained adherence to treatment regimens alongside proactive measures to prevent and manage associated complications. In T2DM, standard management typically involves regular tracking of glucose levels and therapeutic interventions to maintain normoglycemia using oral antidiabetic agents with or without insulin therapy. Current guidelines suggest T2DM treatment strategies that include monotherapy and combination therapies (dual or triple combination) associated with lifestyle modifications[5].

This review article discusses symptoms and diagnostic criteria of T2DM, challenges in glycemic control in primary care, limitations of monotherapy and dual therapy, rationale and advantages of triple combination therapy in association with patient selection criteria, and also addresses side effects and adverse effects. Unless specified otherwise, "Diabetes Mellitus" in this review will denote T2DM for simplicity. It also highlights the algorithms of different international guidelines. Further, it presents an overview of the clinical evidence for the triple combination usage.

SYMPTOMS AND DIAGNOSIS OF DIABETES MELLITUS

The classical symptoms of diabetes mellitus are increased appetite, persistent tiredness, unexpected weight reduction, increased frequency of urination, blurred vision, and delayed wound healing (Fig. 2)[5].

Diagnostic Parameters

A diagnosis of diabetes is established when one or more of the criteria outlined in Table 1 are met. At present, both the IDF[1] and the World Health Organization (WHO)[6] recommend the 75-g oral glucose tolerance

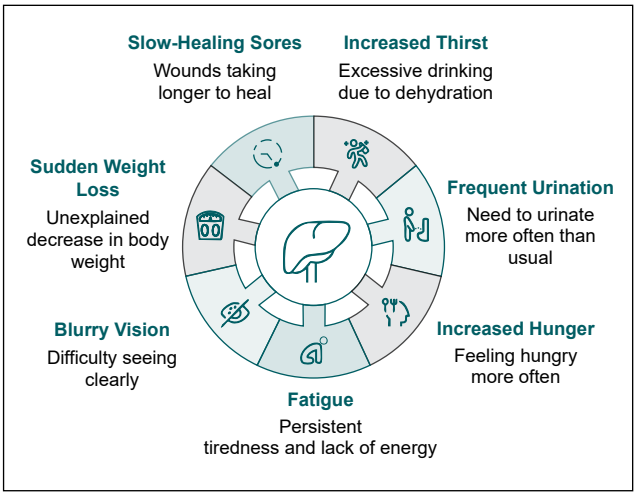


Figure 2. Symptoms of diabetes mellitus.

Table 1. As per the WHO and IDF Recommended Diagnostic Parameters of Diabetes Mellitus[1,6]

Test	Normal	Prediabetes (IFG)	Diabetes
FPG	<110 mg/dL	110-125 mg/dL	≥126 mg/dL
HbA1c	<6.0%	6.0%-6.4% (equivalent)	≥6.5% (equivalent)

WHO = World Health Organization; IDF = International Diabetes Federation; FPG = Fasting plasma glucose; HbA1c = Glycated hemoglobin; IFG = Impaired fasting glucose.

test (OGTT) for diagnosing glucose abnormalities. This test involves measuring fasting plasma glucose (FPG) and the 2-hour value after glucose ingestion to identify conditions such as impaired fasting glucose (IFG), and diabetes (Table 1).

In the case of T2DM, a diagnosis can be established if a random plasma glucose level is >200 mg/dL in the presence of classic symptoms like excessive urination, increased thirst, and unexplained weight loss. Alternatively, a glycated hemoglobin (HbA1c) value exceeding 6.4%, which reflects average blood glucose over the previous 2 to 3 months, also supports the diagnosis[6]. Since HbA1c measurement is not always possible in primary health care facilities, using estimated average glucose provides an alternative means of evaluation.

Table 2 presents a conversion chart correlating HbA1c percentages with estimated average glucose levels.

COMPLICATIONS ASSOCIATED WITH UNCONTROLLED T2DM

Poorly managed T2DM can lead to serious, multi-organ complications[7] (Fig. 3). CVD is a major concern, with up to 22% of individuals with diabetes affected by heart

Table 2. Conversion Chart of HbA1c into Average Blood Glucose Levels

Glycemic category	HbA1c (%)	Estimated average glucose (mg/dL)
Normal	Less than 5.7	Below 117
Prediabetes	5.7-6.4	117-137
Diabetes	Greater than 6.4	Above 137
	6.5	140
	7.0	154
	7.5	169
	8.0	183
	8.5	197
	9.0	212
	9.5	226
	10.0	240

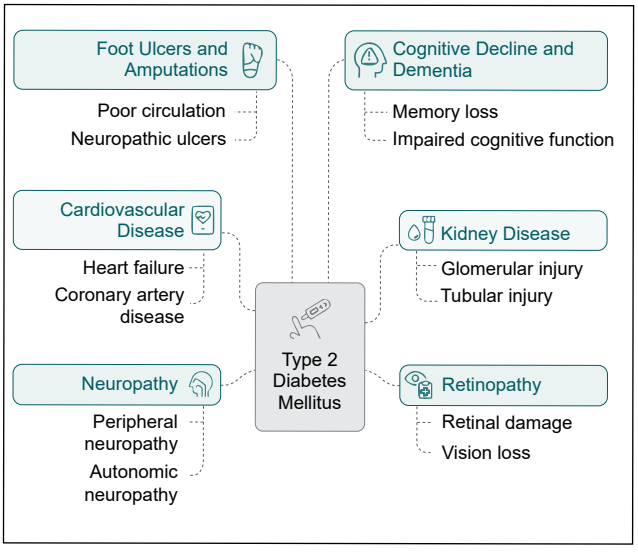


Figure 3. Complications of uncontrolled T2DM.

attacks, strokes, or heart failure[8]. Diabetic nephropathy can progressively damage the kidneys, while diabetic retinopathy continues to be one of the primary causes of vision loss. Neuropathy is another comorbidity, presenting as peripheral nerve damage (pain, numbness in limbs) or autonomic dysfunction affecting the gastrointestinal system, bladder, or sexual function. Foot complications, including ulcers and amputations, often result from a combination of neuropathy and poor circulation. Additionally, individuals with T2DM have a higher likelihood of experiencing cognitive impairment and developing dementia[7].

CHALLENGES IN GLYCEMIC CONTROL IN PRIMARY CARE

Glycemic control in primary care is hindered by multiple challenges, including therapeutic inertia, delayed diagnosis, and limited time for comprehensive diabetes management. Many patients do not receive timely treatment intensification despite poor glycemic control, as noted in American Diabetes Association (ADA)[2], Research Society for the Study of Diabetes in India (RSSDI)[9], and American Association of Clinical Endocrinology (AACE) guidelines[10]. Factors such as poor patient adherence, inadequate access to diabetes education, and lack of routine follow-up further complicate management. Additionally, the limited use of newer therapies, the presence of comorbidities, polypharmacy, and socioeconomic barriers such as affordability and low health literacy contribute to suboptimal outcomes. These challenges underscore the need for a more integrated and proactive approach in primary care settings[11].

LIMITATION OF SINGLE THERAPY AND DUAL COMBINATION THERAPY

While monotherapy with metformin is typically the first-line treatment as per ADA, AACE, and RSSDI guidelines, its effectiveness diminishes over time due to progressive beta-cell dysfunction[12]. It may also be difficult for some individuals to maintain ideal blood glucose levels (including HbA1c), increasing the risk of complications. Since a single drug cannot address all aspects of the disease pathology, its effectiveness is limited, especially in patients with comorbidities like renal impairment or CVD, often necessitating additional medications[12]. Sodium-glucose cotransporter 2 (SGLT2) inhibitors like dapagliflozin may elevate the likelihood of urinary tract and genital infections because of increased glucose excretion in the urine[13].

RSSDI and AACE recommend considering early combination therapy if the baseline HbA1c is ≥7.5% or if blood glucose levels are not met within 3 months of monotherapy[9,10]. While dual therapy offers greater efficacy compared to single-drug treatment, it has its own limitations. Around 40% to 50% of patients may encounter treatment failure within 3 to 5 years[14].

ADA and AACE guidelines highlight that dual therapy may be insufficient for individuals with higher baseline HbA1c (≥9%) or rapid disease progression[2,10]. Moreover, certain drug combinations can lead to an elevated risk of low blood sugar levels or unwanted weight gain. Thus, the guidelines increasingly support early use of triple therapy or incorporation of agents with complementary

mechanisms like glucagon-like peptide-1 receptor agonists (GLP-1RA) or SGLT2 inhibitors to achieve durable glycemic control[2,10].

SETTING THE STANDARD: SMART-DM FOR MEASURABLE DIABETES OUTCOMES

SMART-DM stands for simplified management and actionable recommendations for treating diabetes mellitus. The approach emphasizes setting realistic and personalized glycemic targets, simplifying treatment algorithms, and providing clear, actionable steps for medication initiation and adjustment. SMART-DM encourages regular follow-up, patient education, lifestyle modification, and timely screening for complications all within the scope of primary care. It aims to align real-world practice with established clinical guidelines by promoting structured yet flexible management.

Rationale for Combination Therapy

T2DM is a chronic condition characterized by a gradual decline in insulin sensitivity over time and declining beta-cell function, making monotherapy often inadequate over time. Early combination therapy is more effective than stepwise addition, offering better glycemic control and fewer complications[15].

Combination therapy is characterized by simultaneous targeting of the multiple pathophysiological processes in T2DM. It offers a favorable safety profile, quick action, and ensures long-term glycemic regulation. Additionally, it enhances insulin sensitivity and beta-cell performance, supports weight loss and blood pressure reduction, minimizes the number of medications required, and is economically efficient. Initiating treatment with combinations like metformin plus GLP-1RA or SGLT2 inhibitor helps achieve faster targets and adds cardiorenal benefits[15].

The 2022 European Association for the Study of Diabetes (EASD) and ADA joint consensus reports recommends early combinations for patients with HbA1c ≥8.5% or high-risk comorbidities like CVD, chronic kidney disease (CKD), or heart failure[16]. According to ADA 2023 guidelines, early initiation of triple combination therapy may be considered in patients with markedly elevated HbA1c levels or inadequate glycemic control on dual therapy[17].

The triple combination of sitagliptin, dapagliflozin, and metformin offers a complementary mechanism of action to effectively manage T2DM (Fig. 4). Metformin enhances the body's response to insulin and decreases glucose production by the liver. Sitagliptin (dipeptidyl peptidase-4 [DPP-4] inhibitor) enhances incretin hormones (GLP-1) activity to increase insulin secretion and suppress glucagon, while dapagliflozin (SGLT2 inhibitor) promotes urinary glucose excretion. Together, they provide robust HbA1c reduction with a low risk of hypoglycemia. This combination also supports weight control and offers added cardiovascular and renal protection through the SGLT2 inhibitor[18]. The triple drug combination exhibits synergistic action by targeting different pathways in glucose metabolism.

Advantages of Triple Combination Therapy

Combination therapy in T2DM offers various advantages over monotherapy, particularly when a single drug is insufficient to achieve glycemic targets (Fig. 5). It allows for a more comprehensive approach by addressing multiple steps in the pathogenesis of diabetes, such as insulin resistance, impaired release of insulin and overproduction of glucose by the liver. Additionally, combination therapies contribute to beta-cell preservation by reducing chronic hyperglycemia. These regimens also minimize the pill burden and potential for medication errors, leading to better treatment adherence and compliance. By promoting early and effective treatment

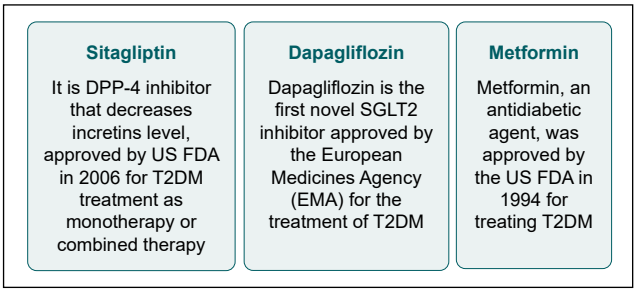


Figure 4. SMART DM: Triple combination therapy; sitagliptin, dapagliflozin, and metformin.

DPP-4 = Dipeptidyl peptidase-4; US FDA = United States Food and Drug Administration; T2DM = Type 2 diabetes mellitus; SGLT2 = Sodium-glucose cotransporter 2.

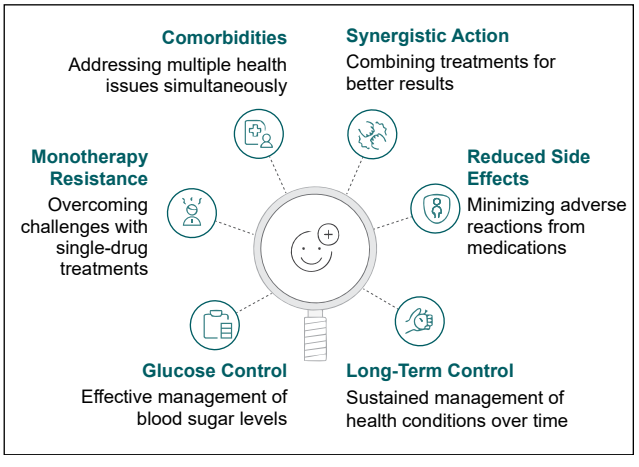


Figure 5. Advantages of triple combination therapy.

initiation, they help avoid clinical inertia, a common barrier in diabetes management. Moreover, such therapies improve overall safety profiles by supporting weight loss, offering CKD and cardiovascular protection, and reducing the risk of hypoglycemia[11]. Lastly, combination therapies have been shown to be cost-effective in the long-term by preventing complications and reducing health care utilization[19].

Pharmacological Synergy and Complementary Mechanisms

The triple fixed-dose combination (FDC) of metformin, dapagliflozin, and sitagliptin offers a scientifically sound and synergistic strategy to regulate T2DM by targeting three distinct but complementary mechanisms (Fig. 6).

Metformin, a biguanide, primarily lowers liver glucose output and improved responsiveness to insulin, and modestly reduces intestinal glucose absorption. It acts independently of insulin secretion, thereby posing a less risk of lower blood sugar level[20]. Dapagliflozin, a SGLT2 inhibitor, lowers the uptake of sugar in the proximal segments of the renal tubules, resulting in glycosuria and reduced plasma glucose levels. Its action is independent of insulin, and it provides additional metabolic benefits such as decrease in weight, reduced systolic blood pressure, and demonstrated cardiovascular and renal protection[21].

Sitagliptin, belonging to the class of DPP-4 inhibitors, works by blocking the breakdown of incretin hormones such as GLP-1 and glucose-dependent insulinotropic polypeptide (GIP). This action helps boost insulin secretion in response to glucose and reduces the release of glucagon. This mechanism helps regulate blood glucose levels effectively in both fasting and post-meal states, while posing a low risk of causing hypoglycemia[22].

In combination, these agents exert a complementary effect; metformin reduces hepatic glucose output, dapagliflozin increases glucose elimination via urine, and sitagliptin improves pancreatic insulin response resulting in better glycemic control without overlapping side effects. This synergy also reduces the likelihood of treatment failure and supports long-term disease management. Urinary tract and genital infections were observed less frequently with triple therapy compared to dapagliflozin combined with metformin or dual therapy. The reduced incidence of genital infections with the combination of an SGLT2 inhibitor and a DPP-4 inhibitor has been previously documented, likely due to the complementary mechanisms of action of these two drug classes[23].

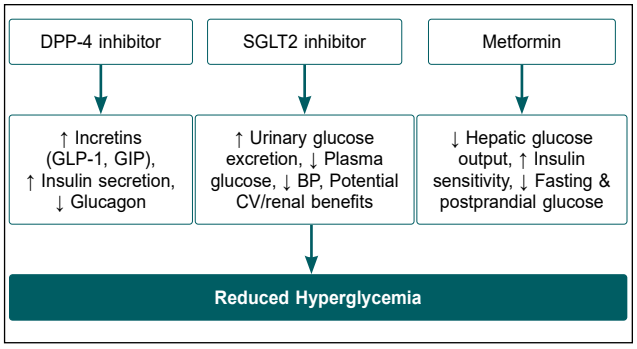


Figure 6. Synergy and complementary mechanisms of triple drug combination therapy.

DPP-4 = Dipeptidyl peptidase-4; GLP-1 = Glucagon-like peptide-1; GIP = Glucose-dependent insulinotropic polypeptide; SGLT2 = Sodium-glucose cotransporter 2; BP = Blood pressure; CV = Cardiovascular.

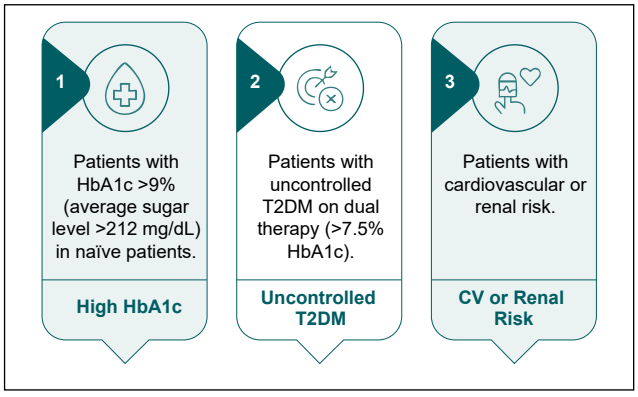


Figure 7. Patient selection criteria for triple combination therapy.

HbA1c = Glycated hemoglobin; T2DM = Type 2 diabetes mellitus; CV = Cardiovascular.

Patient Selection and Practical Considerations

The triple FDC is best suited for individuals with T2DM who are treatment-naïve and present with high HbA1c levels at diagnosis (>8.5% or 9%) or average blood glucose >212 mg/dL, as well as for those who remain poorly controlled despite dual combination therapy (HbA1c >7.5% or average blood glucose level >169 mg/dL)[5]. It is especially useful in patients with existing cardiovascular risk factors warranting early intensive therapy, and in those who struggle with medication adherence, as the single-pill formulation simplifies the regimen and improves compliance (Fig. 7).

Overweight patients may benefit from the weight- and cardiorenal-protective effects of dapagliflozin. The combination should be given only in patients with estimated glomerular filtration rate (eGFR) ≥45 mL/min/1.73 m^2 only. Avoid sitagliptin in patients with history of pancreatitis. In elderly patients, monitor renal function, hydration, and cardiovascular status

closely. In those with cardiovascular risk or CKD, triple FDC may improve glycemia and reduce cardiorenal events; careful patient selection and monitoring remain essential[1,2].

Addressing Safety, Side Effects, and Interactions

The triple combination of metformin, dapagliflozin, and sitagliptin is generally well-tolerated, but it is important to monitor specific safety concerns. Common adverse events include gastrointestinal discomfort with metformin, dehydration with dapagliflozin, and nasopharyngitis or headache with sitagliptin. While the risk of hypoglycemia is low due to the glucose-dependent mechanisms of these drugs, caution is advised when used alongside insulin or sulfonylureas[24]. Drug-drug interactions are minimal but may occur with medications affecting renal function, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or diuretics, which can enhance the risk of dehydration or lactic acidosis. Risk mitigation strategies include regular monitoring of renal function, patient education on hydration, recognizing signs of infection or pancreatitis, and adjusting doses in renal impairment. Overall, proactive assessment and individualized care can enhance the safety of this combination in clinical practice.

CLINICAL PRACTICE GUIDELINES ALIGNMENT

The use of triple therapy in T2DM, particularly combinations like metformin + dapagliflozin + sitagliptin, is well aligned with international guidelines such as those from the ADA-EASD[16] and IDF[1] (Table 3). These guidelines recommend a stepwise or early combination approach based on the individual patient's profile, including glycemic targets, presence of comorbidities (e.g., atherosclerotic cardiovascular disease [ASCVD], CKD, heart failure), and risk of hypoglycemia or weight gain[1,2].

The ADA-EASD consensus endorses early use of combination therapies in individuals with HbA1c >1.5% above target or in those with high-risk features, emphasizing the use of SGLT2 inhibitors and/or DPP-4 inhibitors based on clinical need[16]. Similarly, IDF[1] guidelines recommend combination therapy when monotherapy fails or at diagnosis in patients with high HbA1c. Indian national guidelines also reflect this approach, promoting personalized treatment strategies, especially in patients with cardiorenal risk or those needing durable glycemic controls[9]. The triple FDC aligns well with these guidelines by combining complementary mechanisms (hepatic, renal, and incretin pathways), minimizing hypoglycemia risk, and improving adherence through a simplified regimen[25].

CLINICAL EVIDENCE SUPPORTING TRIPLE FDC USE

This section presents an overview of the clinical evidence for the triple combination therapy of sitagliptin, dapagliflozin, and metformin (Table 4).

The MESIDA trial, a Phase 3 randomized study in Indian adults with type 2 diabetes, compared a triple therapy (dapagliflozin, sitagliptin, metformin – DSM) to a dual therapy (sitagliptin, metformin – SM). Over 16 weeks, DSM led to significantly greater HbA1c reduction (−1.45% vs. −1.00%; p = 0.0005) (Fig. 8), along with better FPG and postprandial plasma glucose (PPG)

Table 3. Guideline Recommendations for the Use of Triple Combination Therapy in Diabetes Mellitus

Guideline	Recommendation on combination therapy	Suggestions for triple FDC	Comments
ADA (2026)[2]	Recommends dual or triple therapy if HbA1c >1.5% above target; prioritizes SGLT2i/ DPP-4i in patients with ASCVD, CKD, or HF	Supports triple FDC in uncontrolled patients or high-risk groups	Emphasizes individualized, comorbidity-focused care
ADA-EASD (2024)[16]	Advocates early combination for high HbA1c or comorbidities; recommends SGLT2i/ DPP-4i post-metformin	Triple FDC fits as a preferred option after metformin monotherapy or dual therapy failure	Cardiorenal benefit prioritized
IDF (2025)[1]	Combination therapy recommended when monotherapy fails; consider CV and renal risk	Triple FDC aligns with guidelines, especially for broader accessibility	Encourages cost-effective and simplified regimens
India (RSSDI)[9]	Endorses stepwise escalation or early combination; dual oral therapy for uncontrolled cases	Triple FDC recommended in cases with poor adherence, obesity, or comorbidities	Tailored to Indian phenotype and affordability

FDC = Fixed-dose combination; ADA= American Diabetes Association; HbA1c = Glycated hemoglobin; SGLT2i = Sodium-glucose cotransporter 2 inhibitor; DPP-4i = Dipeptidyl peptidase-4 inhibitor; ASCVD = Atherosclerotic cardiovascular disease; CKD = Chronic kidney disease; HF = Heart failure; EASD = European Association for the Study of Diabetes; IDF = International Diabetes Federation; CV = Cardiovascular; RSSDI = Research Society for the Study of Diabetes in India.

Table 4. Overview of Clinical Trial of Triple Combination Therapy with Primary Outcomes and Key Results

Study/Year	Design/Phase	Population	Intervention	Comparator(s)	Key findings	Authors
MESIDA Trial (2024)	Phase 3, multicenter RCT	274 Indian adults with T2DM	Dapagliflozin (10 mg) + Sitagliptin (100 mg) + Metformin ER (1,000 mg) FDC (triple)	Sitagliptin (100 mg) + Metformin SR (1,000 mg) FDC (dual)	Superior HbA1c, FPG, PPG reduction; optimal safety profile	Singh et al[26]
Open-Label Study (2023)	Phase 3, randomized, open-label	Patients with HbA1c ≥8% and ≤11%	Dapagliflozin + Sitagliptin+ Metformin ER FDC (triple)	Sitagliptin + Metformin SR and Dapagliflozin + Metformin ER	Triple FDC superior glycemic control	Sahay et al[24]
Controlled Trial (2025)	Phase 3, randomized	274 T2DM not controlled with metformin	Dapagliflozin (10 mg) + Sitagliptin (100 mg) + Metformin XR (1,000 mg) FDC (triple)	Sitagliptin + Metformin XR FDC (dual)	Greater efficacy for glycemic targets; similar safety	Singh et al[18]
Bioequivalence Trial (2024)	Open-label, crossover PK	24 healthy male volunteers	Dapagliflozin + Sitagliptin + Metformin ER FDC (triple)	Sitagliptin (100 mg); Dapagliflozin + Metformin ER (dual)	Bioequivalence; established safety, tolerability	Dhar et al[19]

RCT = Randomized controlled trial; T2DM = Type 2 diabetes mellitus; ER = Extended release; FDC = Fixed-dose combination; SR = Sustained release; HbA1c = Glycated hemoglobin; FPG = Fasting plasma glucose; PPG = Postprandial plasma glucose; XR/ER = Extended release; PK = Pharmacokinetic.

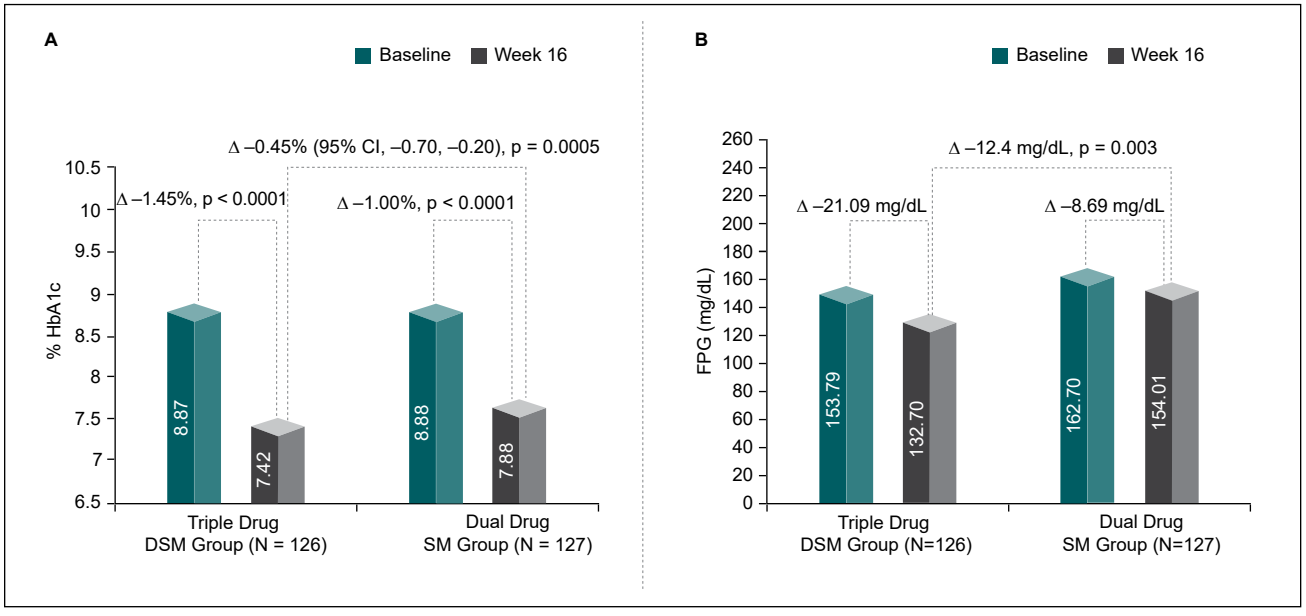


Figure 8. Changes in **A**) HbA1c; **B**) FPG levels after 16 weeks after administering DSM (triple drug) and SM (dual drug)[26].

control. Weight changes and tolerability were similar in both groups, with DSM offering superior glycemic control[26].

A Phase 3 study in adults with type 2 diabetes poorly controlled on metformin (HbA1c 8%-11%) compared a triple FDC (dapagliflozin, sitagliptin, metformin) to two dual therapies (sitagliptin + metformin SR and dapagliflozin + metformin ER). At 16 weeks, the triple therapy led to a greater HbA1c reduction (−1.73%) than either dual option (−1.28% and −1.33%; $p < 0.001$) (Fig. 9). It also improved FPG and PPG levels, with more patients reaching HbA1c <7%. The triple combination offered superior glycemic control without added safety risks[24].

Dhar et al demonstrated that the FDC of dapagliflozin, sitagliptin, and metformin XR is bioequivalent to the reference formulations under fed conditions in Indian adults. These results support its use as a convenient and effective treatment option for improving glycemic control in type 2 diabetes within the Indian clinical setting[19].

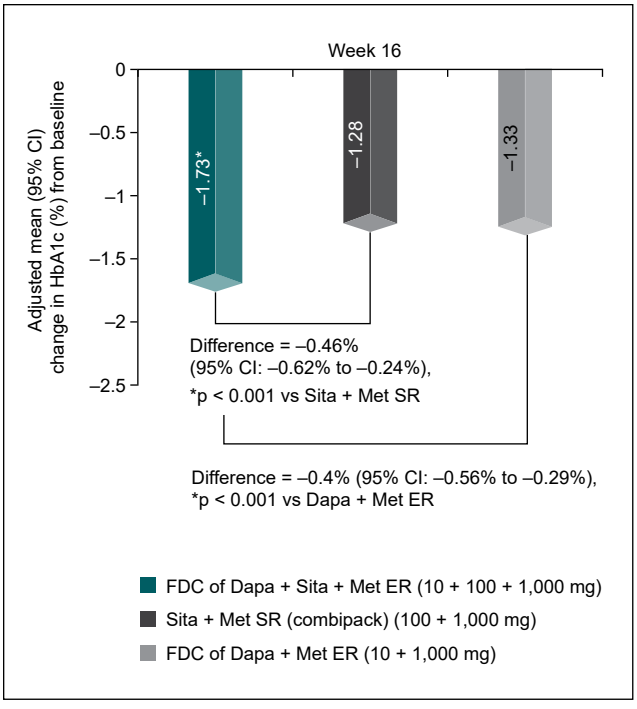


Figure 9. HbA1c level of triple combination (Dapagliflozin + Sitagliptin + Metformin), Sitagliptin + Metformin SR, and FDC Dapagliflozin + Metformin ER after 16 weeks[24].

CONCLUSION

The effective management of T2DM requires a proactive and individualized treatment approach that addresses the multifactorial nature of the disease. While monotherapy and dual therapy remain important components of initial care, their limitations often lead to suboptimal glycemic control and increased risk of complications over time. Early initiation of triple combination therapy particularly with agents such as metformin, dapagliflozin, and sitagliptin offers a comprehensive strategy to target key pathogenic pathways, enhance glycemic durability, and minimize treatment-related risks such as hypoglycemia and weight gain.

The fixed-dose triple regimen not only simplifies patient adherence but also aligns well with current international and national guidelines. By incorporating cardiorenal protective effects and improving long-term outcomes, this combination represents a rational and evidence-based advancement in diabetes care.

Adoption of simplified frameworks like SMART-DM can further support primary care providers in delivering consistent, guideline-driven, and patient-centered treatment. Overall, triple combination therapy marks a significant step forward in closing the gap between clinical recommendations and real-world practice.

Conflict of Interest

The authors declare that there is no conflict of interest related to the publication of this review.

Disclaimer

The term "SMART DM" used in the title and throughout this manuscript is an abbreviation created for the purposes of this review solely. It does not refer to, nor is it associated with, any existing product, brand, trademark, or commercial entity.

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