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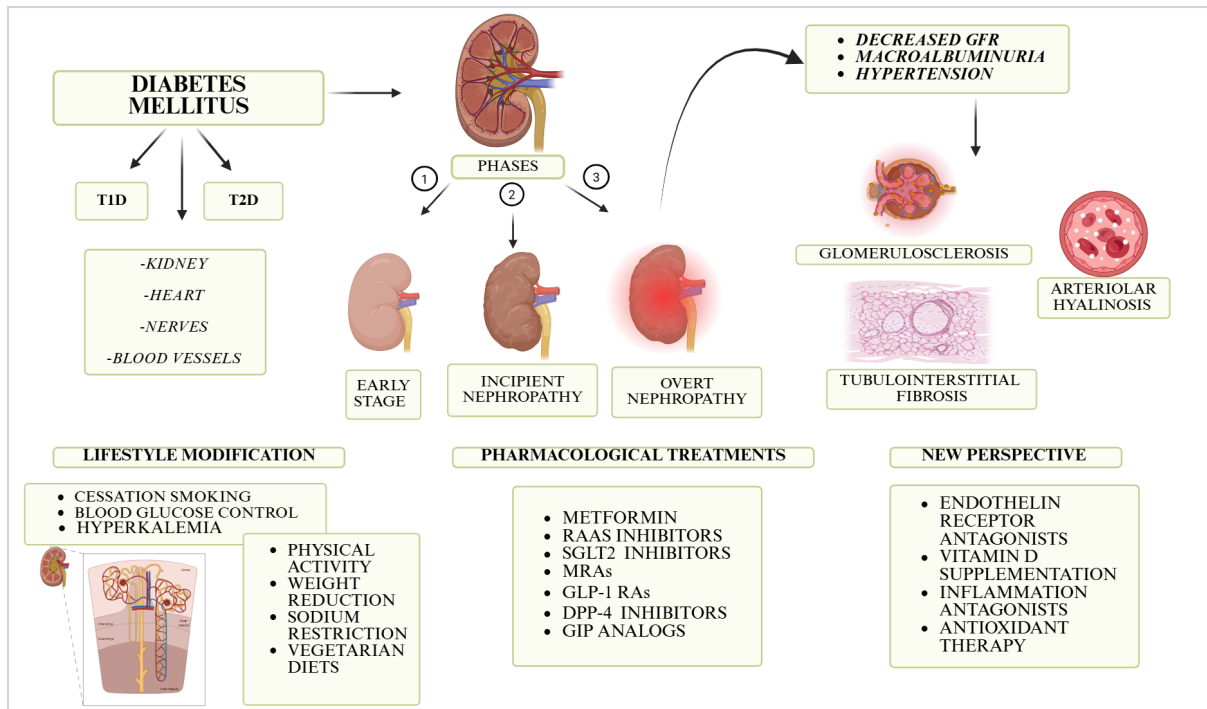
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Supplementary Table 1 Summary of main pharmacological classes used in the management of Diabetic Kidney Disease, highlighting their mechanisms of action, representative molecules, and clinical effects

Pharmacological class	Mechanism of action	Molecule	Effectiveness	Outcomes	Contraindications/Side effects	Ref.
Biguanides	Not completely understood	Metformin	Hepatic gluconeogenesis ↓ Intestinal glucose absorption ↓ Peripheral glucose uptake ↑ Fatty acid oxidation ↓ LDL and triglycerides levels ↓ Obesity ↓	Nephroprotective Vasculoprotective Anti-inflammatory Anti-fibrotic Slowing CKD progression	Gastrointestinal Lactic acidosis Hypoglycemia (rare)	[47-48]
ACE inhibitors	RAAS system inhibition;	Enalapril, Ramipril	↓ glomerular pressure; ↓ proteinuria; ↓ GFR;	slows CKD progression;	hyperkalemia; bilateral renal artery stenosis;	[60-61-62]
SGLT2i	Inhibition of Na-Glucose transporter	Dapagliflozin, Empagliflozin, Canagliflozin	Natriuria ↑ Glycosuria ↑ Albuminuria, proteinuria ↓ UACR ↓ Intraglomerular pressure ↓ Blood pressure ↓ Obesity ↓	Nephroprotective Cardioprotective Anti-inflammatory Anti-fibrotic Slowing CKD progression	Ketoacidosis	[56-64]
MRAs (Steroids)	Mineralocorticoid receptor antagonism	Spirolactone, Eplerenone	Proteinuria ↓ Albuminuria ↓	Nephroprotective Cardioprotective Slowing CKD/DKD progression	Gynecomastia Menstrual irregularities Hyperkalemia	[65-72]

MRAs steroids)	(Non Mineralocorticoid receptor antagonism	Aparenone, Hexaxerenone  AZD-9977 (Phase II) KBP-5074, BI690517 (ongoing phase)	Proteinuria ↓ Albuminuria ↓	Nephroprotective Cardioprotective Anti-inflammatory Anti-fibrotic	Hyperkalemia	[73]
GLP-1 RAs	Stimulation of insulin secretion Inhibition of glucagon production	Liraglutide, Dulaglutide	Semaglutide, Glucose-dependent insulin. ↑ Glucagon ↓ Albuminuria. ↓	Nephroprotective Cardioprotective Anti-inflammatory Anti-atherogenic Endothelial-protective	Pancreatitis Gastroparesis Medullary thyroid carcinoma	[83-87]
DPP- 4 i	Inhibition of the degradation of GLP-1 and GIP thereby enhancing insulin secretion and suppressing glucagon release	Sitagliptin, Vildagliptin, Alogliptin,	Linagliptin, Insulin ↑ Glucagon glucose- dependent ↓ Albuminuria ↓	Nephroprotective Cardioprotective	Gastrointestinal	[88-95]
GLP1/GIP a	PI3K-AKT survival pathway activation	Tirzepatide	Glicemic control ↑ Obesity ↓ Albuminuria ↓ UACR ↓	Nephroprotective Anti-inflammatory Slowing GFR decline	Gastrointestinal	[96-99]

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It focuses on renal and cardiovascular outcomes, including nephroprotection, reduction of albuminuria/proteinuria, and slowing of renal disease progression, together with key adverse effects and contraindications. GLP-1 RAs: Glucagon-like peptide-1 receptor agonists; DPP-4i: Dipeptidyl peptidase-4 (DPP4) inhibitors; GLP1/GIPa: Glucose-dependent insulintropic polypeptide analogs; MRAs: Mineralocorticoid receptor antagonist; SGLT2i: Sodium-glucose co-transporter inhibitors; UACR: Urine Albumin-to-creatinine ratio.