• **Insulin secretagogues:** These category of drugs (especially sulfonylureas and metiglinides) act by increasing the secretion of insulin from pancreas by binding to sulfonylurea receptor (SUR) of ATP sensitive potassium channel on pancreatic β cells.

1st generation sulfonylurea are Tolbutamide, Chlorpropamide, Tolazamide, Acetohexamide and

2nd generation sulfonylurea includes Glibenclamide, Glipizide, Glimepiride. Development of 2nd generation sulfonylurea was due to increased potency, more rapid onset of action, shorter plasma half-lives and longer duration of action.

Common side effects of sulfonylurea includes sign of low blood sugar level such as dizziness, sweating, confusion and nervousness. It may also include hunger, weight gain, skin reaction, stomach upset and dark coloured urine.

Metiglinide is the prototype molecule that is a derivative of benzoic acid of non-sulfonylurea moiety of Glibenclamide. These agents exert their effect by closing the ATP sensitive potassium channel found on plasma membrane of pancreatic β cells. Other molecules used in this category are Repaglinide and Nateglinide

Repaglinide, an oral insulin secretagogue, was the first prandial glucose regulator (PGR) to be licensed and has been available since 1998. It differs structurally from SUs as it is a carbamoylmethyl benzoic acid derivative. It is structurally related to meglitinide Repaglinide binds to the sulphonylurea receptor and to its own distinct binding site on the pancreatic beta-cell

Sulphonylureas (SU) have been the mainstay of treatment for type 2 diabetes and remain the most commonly prescribed first-line oral hypoglycaemic agent (OHA). They are insulin secretagogues and bind to a sulphonylurea receptor on the b-cell. This leads to depolarization of the b-cell membrane and stimulation of insulin. Both chlorpropamide (a firstgeneration sulphonylurea) and

glibenclamide and gliclazide (second generation SUs) have good efficacy and outcome data.

The Sulfonylurea Receptor

Insulin secretagogues of the sulfonylurea class have been the mainstay of oral therapy for type 2 diabetes for many years. It has been known for some time that these agents stimulate insulin secretion by blocking an ATP-sensitive K^+ channel (KATP) in the pancreatic β-cell leading to membrane depolarization, elevation in intracellular Ca^{2+} and insulin granule exocytosis. Recently, new insight into the mechanism of action of this class of compounds has been gained following the cloning and expression of its molecular target, the sulfonylurea receptor (SUR). A thirteen membrane spanning protein of the ATP-binding cassette superfamily, the SUR multimerizes with an inward rectifier type K channel (kir 6.2) to form an ATP-sensitive K channel. This area has been recently reviewed.

Sulphonylureas, because of their potential risk of hypoglycaemia, have to be used in conjunction with a regimented dosage and dietary regime. Thus patients are advised to have snacks between main meals, and that missing or delaying a meal can lead to hypoglycaemia.