Oral hypoglycemic agents

Disclaimer

All the content material provided here is only for teaching purpose.

Oral Hypoglycaemic Agents

These drugs lower blood glucose levels and are effective orally. The chief draw back of insulin is—it must be given by injection.

Classification:

1. Sulfonyl ureas:

- First generation: Tolbutamide, Chlorpropamide
- Second generation: Glibenclimide, Glypizide, Gliclazide, Glimepiride

2. Biguanides: Phenformin, Metformin

3. Meglitinide analogues: Repaglinide, Nateglinide

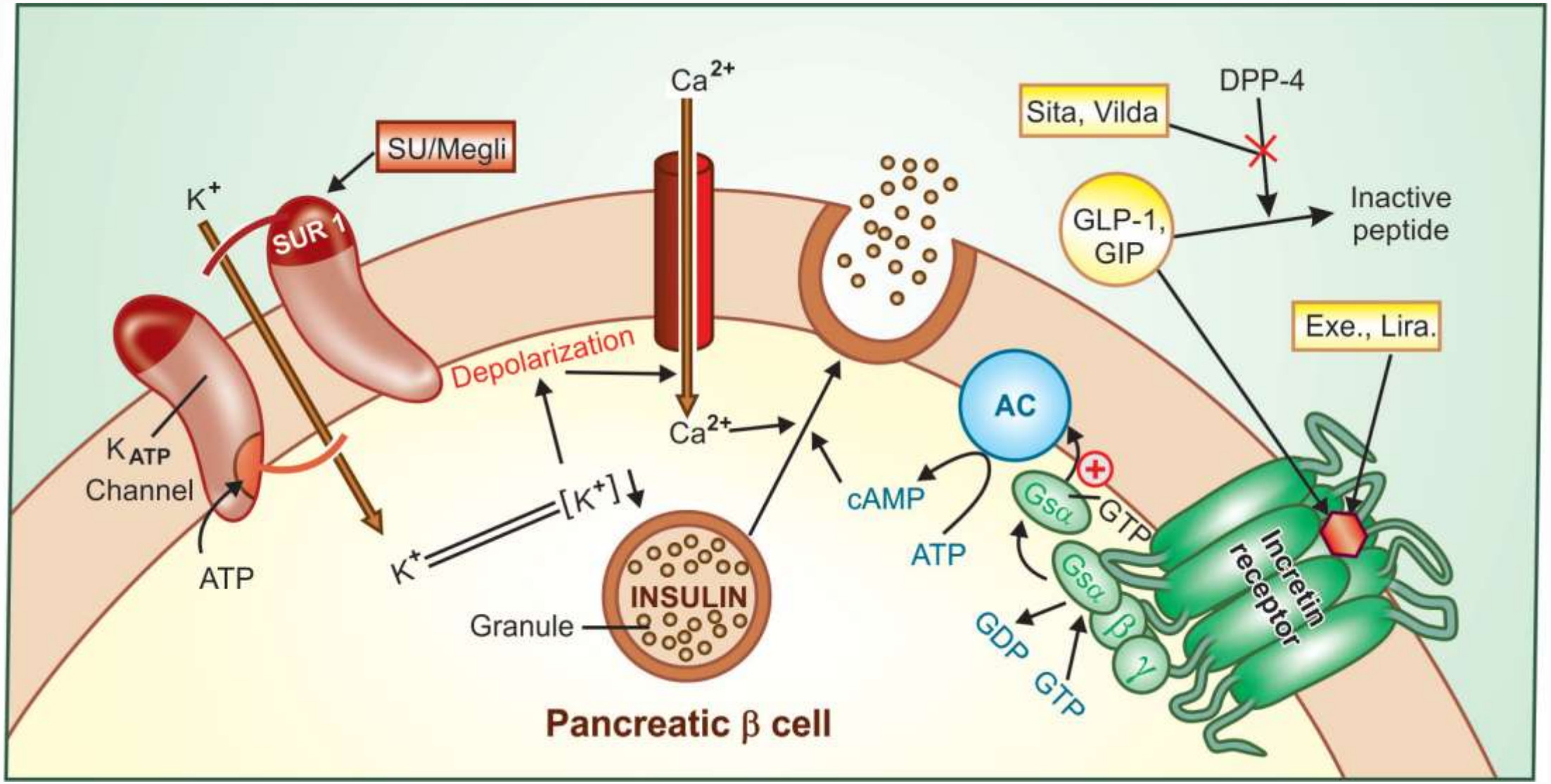
4. Thiazolidinediones: Rosiglitazone, Pioglitazone

5. α Glucosidase inhibitors: Acarbose, Miglitol

Sulfonylureas (K_{ATP} Channel blockers)

All SUs have similar pharmacological profile, their sole significant action being lowering of blood glucose level in normal subjects and in type 2 diabetics, but not in type 1 diabetics.

MOA- The sulfonylureas (SU) and meglitinide analogues (Megli) block the sulfonylurea receptor (SUR1) which constitutes a subunit of the inwardly rectifying ATP-sensitive K+ channel (KATP) in the membrane of pancreatic β cells. The inward flow of K+ ions is thereby restricted, intracellular K+ concentration falls and the membrane is partially depolarized augmenting Ca2+ channel opening as well as release of Ca2+ from intracellular stores. The Ca2+ ions promote fusion of insulin containing intracellular granules with the plasma membrane and exocytotic release of insulin.


Ca2+
SU/Megli
K+
SUR 1
DPP-4
Sita, Vilda
Inactive peptide
GLP-1, GIP
Exe., Lira.
Depolarization
KATP Channel
ATP
[K+]
K+
Ca2+
INSULIN
Granule
AC
cAMP
ATP
Gsα
GTP
Gsα
β
γ
GDP
GTP
Incretin receptor
Pancreatic β cell

Pharmacokinetics:

- All SUs are well absorbed orally
- Low volumes of distribution (0.2–0.4 L/kg)
- The metabolites (active/inactive) are excreted in urine

Adverse effect:

Hypoglycaemia

Hypersensitivity

Nausea, vomiting, flatulence, diarrhoea or constipation, headache and paresthesiasare generally mild and infrequent

References

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