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R E S E A R C H A R T I C L E

Review on Diabetes Medicine: Sulphonylurea

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A B S T R A C T

This article is about "Diabetes Medicine: Sulphonylurea". In this article give information on sulphonylurea which are said to be as "oral hypoglycemic agents" and also about its generation. This article also gives information about 'the way of taking sulphonylurea, its side effect and its action.

Keywords: Diabetes Medicine, Oral hypoglycemic agents, Sulphonylurea

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

Type 1 diabetes, the pancreas no longer makes enough insulin. Insulin is a hormone that helps glucose move from the bloodstream into your cells where the glucose is used for energy. Everyone who has Type 1 diabetes must take insulin, whether by injection, inhalation (for rapid-acting insulin), or insulin pump, to survive. There is no "insulin pill," at least at this time. People with Type 1 Diabetes don't produce insulin. You can think of it as not having a key. With Type 2 diabetes, the situation is a bit different. In the early stages of Type 2 diabetes, the body makes plenty of insulin, but has a hard time using it. This is called insulin resistance. People with Type 2 Diabetes don't respond to insulin as well as they should and later in the disease often don't make enough insulin. You can think of this as having a broken key. Certain medicines, such as metformin, can help improve insulin resistance so that the body can use insulin better. But as Type 2 diabetes progresses, the pancreas can get tired and stop making enough insulin to keep up with the demand. If and when this happens, insulin injections are usually needed.

Sulfonylureas:

Sulfonylureas are the oldest type of diabetes pills available. They were developed in the 1940's and werethe first type of diabetes pill to enter the market. These pills, which are sometimes called "oral hypoglycemic agents," work very differently than metformin. They signal the pancreas to

release insulin and they also help the body's cells use insulin better. Sulfonylureas may be old, but they're effective: They can lower A1C levels (a measure of blood sugar control over the previous 2–3 months) by 1% to 2%. There are two generations of sulfonylureas: first and second.

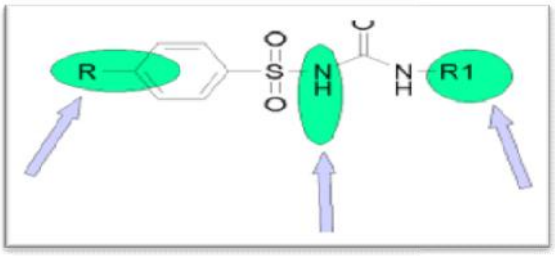


Fig 1: Basic structure of Sulfonyl area

The first-generation includes

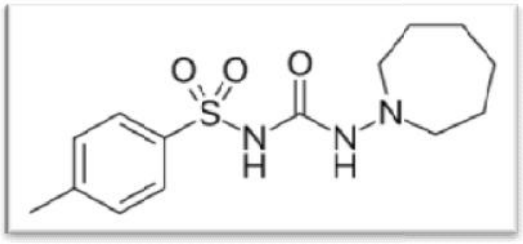


Fig 2: Tolazamide (Tolinase)

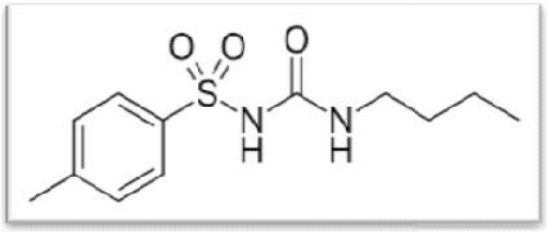


Fig 3: Tolbutamide (brand name Orinase)

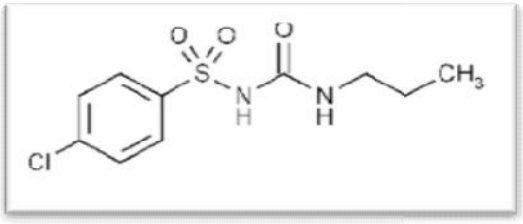


Fig 4: Chlorpropamide (Diabinese)

The second-generation drugs, which are more commonly used these days, include

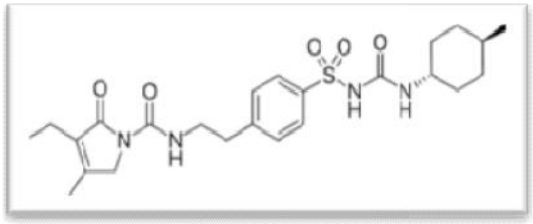


Fig 5: Glimepiride (Amaryl)

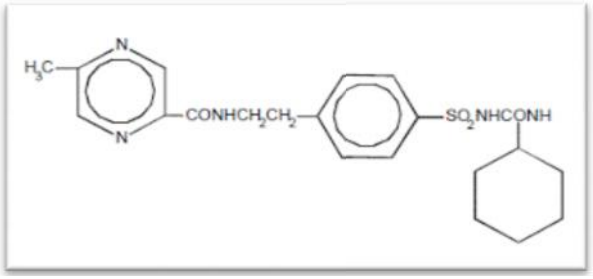


Fig 6: Glipizide (Glucotrol and Glucotrol XL)

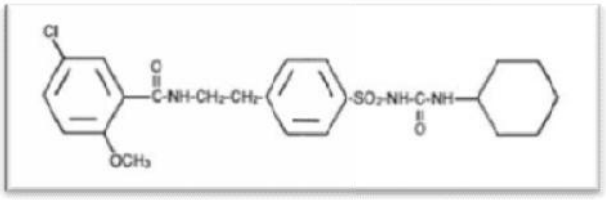


Fig 7: Glyburide (Diabeta, Micronase, and Glynase)

Sulfonylureas are often taken with other types of diabetes medicines, such as metformin and insulin. They're also available as combination pills; for example, combined with metformin (Metaglip).

Dose:

Sulfonylureas are tablets that are taken anywhere from once a day to twice a day. Each type of sulfonylurea is available in different dosages or strengths. In general, your doctor will start you off on the lowest dose and gradually increase the dose, as needed, until your blood sugars come into target range.

Side Effects:

The most common and serious side effect of these drugs is low blood sugar (hypoglycemia). To avoid this, it's important that you not skip meals when taking these medicines. Another possible side effect is weight gain, likely due to increased insulin secretion. Less common side effects include a skin rash and stomach upset. Sulfonylureas may not be safe for people who have liver or kidney problems. One of the drugs in this class, glyburide, may be safe for pregnant women with diabetes who choose not to take insulin; however, sulfonylureas are not deemed safe for nursing women. Up to 20% of people who take these drugs won't respond to them; in other words, they won't help to significantly lower blood sugar levels. For some other people, these drugs may work initially, but over time, they'll become less effective. It's important to check your blood sugar levels regularly when taking a sulfonylurea.

Make sure you know the signs and symptoms of low blood sugar (dizziness, light headedness, shakiness, sweating, headache, hunger) and how to treat it (take 15 grams of carbohydrate, such as 3–4 glucose tablets, a tube of glucose gel, or 4 ounces of juice; wait 15 minutes to recheck your blood sugar, and treat again if it is still low). If you are having frequent low blood sugars, let your doctor know; you may need a lower dose. Your skin may be more sensitive to sunlight while on these drugs. Be sure to use adequate sun protection.

Pharmacogenetic factors that affect drug metabolism and efficacy in type 2 DM:

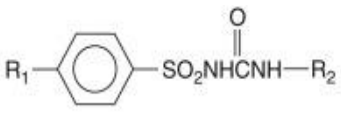
Sulphonylureas are the first OADs to be used but irrespective of novel pharmacological concepts. Sulphonylureas act at the pancreatic β-cell membrane by closing ATP-sensitive potassium channels, which leads to an enhanced insulin secretion independent of glucose. Sulphonylureas can dramatically improve glycemic control and should be considered as the initial treatment for patients with poor glycemic control on an appropriate diet (Pearson et al., 2000). Oral sulphonylurea therapy is safe and effective for a short term in most patients and may successfully replace treatment with insulin injection (Rafiq et al., 2008). The polymorphic enzyme cytochrome P4502C9 (CYP2C9) and 2C19 (CYP2C19) are the main enzymes that catalyze the biotransformation of sulphonylureas. Mutations in KCNJ11, KCNQ1, and HNF1A also affect the clinical use of sulphonylureas.

Therapeutic Areas:

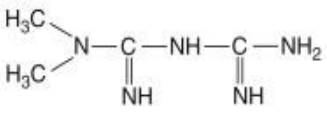
Sulphonylureas increase endogenous insulin secretion. Their efficacy, measured by the plasma glucose lowering effect, is greatest in individuals with newly diagnosed T2DM. Clinical studies have shown that sulphonylureas reduce mean FPG to 54–72 mg dL−1 and HbA1Clevels by 1.5–2%. The benefit of sulphonylurea therapy depends on the initial degree of hyperglycemia, duration of diabetes (more effective in T2DM of shorter duration), and previous use of other oral hypoglycemic agents. Because many of the sulphonylurea metabolites are active, more conservative dosing is advised in any patient who may be at high risk for decreased hepatic metabolism or renal clearance of the active drug or metabolites.

Insulin, Oral hypoglycemics, and Glucagon:

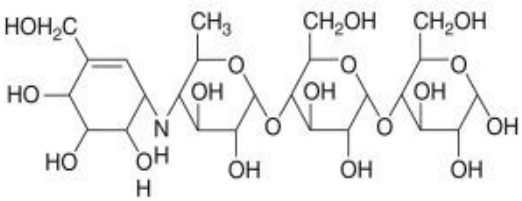
Sulphonylureas are sulfonamide derivatives. They are traditionally divided into two groups or generations of agents. Second-generation sulphonylureas are considerably more potent than the earlier drugs.



General structure of sulfonylureas



Metformin



Acarbose

Figure 8

Drugs That Increase the Effect of sulphonylureas:

Antihistamines (H2 antagonists), Azole antifungals, Clofibrate, Mg++ salts, Methyldopa, Monoamine oxidase inhibitors, Oral anticoagulants, Salicylates, Sulfonamides, Tricyclic antidepressants and β-Adrenergic receptor blockers.

Drugs That Decrease the Effect of sulphonylureas:

Ca2+ salts, Corticosteroids, Diazoxide, Estrogens, Phenothiazines, Sympathomimetics, Thiazide diuretics and Thyroid hormones.

Contraindications:

Contraindications to the use of Sulphonylureas include hypersensitivity to Sulphonylureas and drugs that have similar structures (see earlier) and pregnancy. Caution should be exercised in cases of reduced renal or hepatic function. Patients with ketoacidosis should receive insulin, not an oral anti-hyperglycemic agent.

Mechanism of action:

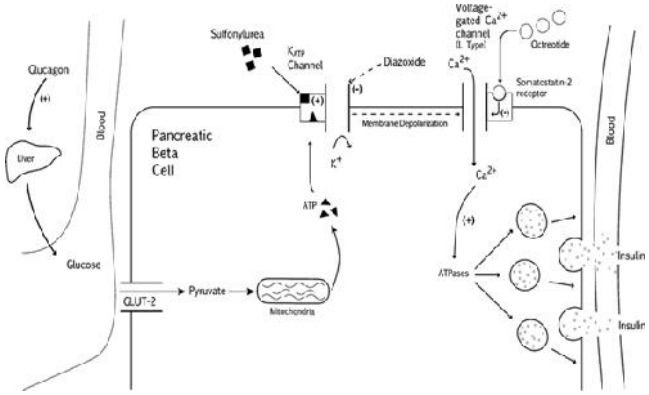


Figure 9

Sulphonylureas are effective only in patients with functioning pancreatic β cells. These drugs stimulate release of insulin by blocking adenosine 5′-triphosphate (ATP)–dependent K+ current in pancreatic β cells. The effects of sulphonylureas are initiated by their binding to and blocking an ATP-sensitive K+ channel. Glimepiride has been shown to have an additional effect: it increases the sensitivity of peripheral tissues to insulin. This may be true for the other sulphonylureas (especially second-generation drugs) as well. The predominant effect is on insulin secretion.

Pharmacokinetics:

Sulphonylureas are well absorbed after oral administration. Glipizide absorption is delayed by food. All sulphonylureas are highly bound to plasma protein (90% to 99%). Plasma protein binding is least for chlorpropamide and greatest for glyburide. Sulphonylureas are metabolized in the liver and excreted in the urine.

The half-lives and extent of metabolism vary considerably among first-generation sulphonylureas. Metabolism of chlorpropamide is incomplete, and approximately 20% of the drug is excreted unchanged, which can be a problem for patients with impaired renal function.

Therapeutic uses:

Sulphonylureas are used to control hyperglycemia in type 2 diabetics who cannot achieve appropriate control with changes in diet and exercise alone.

Adverse effects:

Adverse effects are infrequent, occurring in approximately 4% of patients taking first-generation drugs and perhaps slightly less often in patients receiving second-generation agents. The most important adverse effect is hypoglycemia, which, if severe, can lead to coma. Hypoglycemia is a particular problem in elderly patients with impaired hepatic or renal function who are taking longer acting sulphonylureas. Sulphonylureas have a sulfonamide structure, which is the basis for cross-sensitivity with antibacterial sulfonamide drugs. Hypersensitivity reactions occur with some regularity. Other adverse effects of sulphonylureas include nausea and vomiting, occasional hematologic reactions (especially leukopenia and thrombocytopenia, and hemolytic anemia in susceptible patients), cholestatic jaundice, and dermatologic effects. Sulphonylureas are teratogenic in animals (large doses). Patients taking sulphonylureas tend to gain weight, which is a problem in type 2 diabetics, who tend to be obese.

Sulphonylureas have a disulfiram-like effect. In patients who take alcohol concurrently, sulphonylureas may decrease aldehyde dehydrogenase, causing acetaldehyde accumulation. As a result, the patient may have flushing, headache, nausea, vomiting, sweating, and hypotension shortly after alcohol ingestion. This reaction is not as likely to occur with a single occasional drink.

Drug interaction

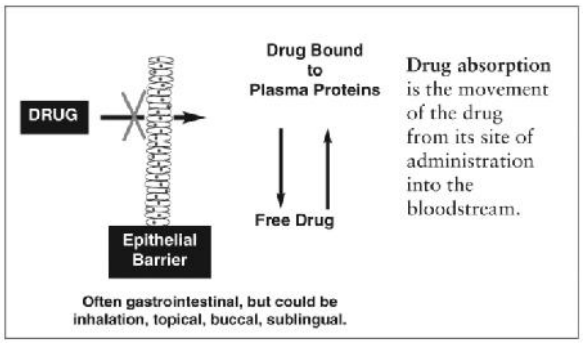


Figure 9

Numerous drugs interact with sulphonylureas by enhancing or decreasing their effect on blood glucose concentration

2. Conclusion

In this article give information on sulphonylurea which are said to be as “oral hypoglycemic agents” and also about its generation. This article also gives information about ‘the way of taking sulphonylurea, its side effect and its action.

Table 1: Oral hypoglycemics

Nonproprietary (Generic) Name	Proprietary (Trade) Name	Onset (hr)	Serum Half-Life (hr)	Duration of Action (hr)
First-Generation				
Chlorpropamide	Diabinese	1	36	24-60
Tolazamide	Tolinase	4-6	7	12-24
Second-Generation				
Glimepiride	Amaryl	2-3	9	10-24
Glipizide	Glucotrol, Glucotrol XL	1-3	2-4	10-24
Glyburide	Diaβeta, Micronase, Glynase PresTabs	1-4∗	4-10	10-24

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