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Pharmacologically relevant drug interactions of sulfonylurea antidiabetics with common herbs

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ABSTRACT

Introduction: Sulfonylurea antidiabetics are insulin secretogogues useful in the treatment of type 2 diabetic patients. The probability of adverse drug interactions is high in patients taking sulfonylureas and other drugs including herbal medicines. The present review is aimed to present the herbal drugs having interacting potentials with sulfonylurea antidiabetics.
Methods: The databases such as PubMed, Google Scholar, Science Direct, Directory of open access journals (DOAJ) and reference lists were searched using the keywords drug interactions, Sulfonylureas, pharmacodynamic interactions, antidiabetic herbs, pharmacokinetic interactions and CYP2C9.
Results: Sulfonylureas are primarily metabolized by CYP2C9 enzyme and the herbs like St. John's wort and *Ginkgo biloba* induce CYP2C9-mediated metabolism of sulfonylureas while fruit juices like Pomegranate juice and Pineapple juice inhibit their metabolism. In addition, the antidiabetic herbal supplements such as Bitter melon, Fenugreek, Cinnamon, Gymnema, Ginseng, Ginger, Garlic, *Aloe vera,* Sesame, *Andrographis paniculata* and Neem potentiate the hypoglycemic activity of sulfonylureas, pharmacodynamically.
Conclusion: Some herbal supplements are capable of interacting pharmacokinetically and pharmacodynamically with sulfonylurea antidiabetics

Implication for health policy/practice/research/medical education:
Due to the possible interaction of herbal supplements with sulfonylurea antidiabetics, prescribers and pharmacists are required to be aware of these drug interactions to avoid the possible problems for patients.
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Introduction

Diabetes mellitus (DM) is a chronic metabolic condition in which hyperglycemia is noted for a longer duration (1). It is a global health burden and the incidence of diabetes among global population is increasing every year. It has been estimated that 171 million of world population were affected by diabetes in the year of 2000 (2), 285 million in 2010 (3), 366 million in 2011 (4), 382 million in 2013 (5), 415 million in 2015 (6) and 451 million in 2017 (7). The prevalence of diabetes around the globe has been projected as 552 million by 2030 (8), 592 million by 2035 (9), 642 million by 2040 (10) and 693 million by 2045 (11). DM is sorted mainly as type 1 DM which is insulin-dependent (IDDM) and type 2 DM, the non-insulin dependent (NIDDM). DM could be managed by both non-pharmacological and pharmacological therapies. Non-pharmacological management of diabetes includes lifestyle modifications such as dietary interventions, increased physical activity and smoking cessation. (12). Type 1 diabetes is managed pharmacologically by administering insulin injections mainly and the pharmacological management of type 2 diabetes includes the use of antidiabetic medications such as metformin, sulfonylureas, meglitinides (repaglinide and nateglinide), thiazolidinediones (rosiglitazone and pioglitazone), alpha glucosidase inhibitors (acarbose and miglitol), dipeptidyl peptidase 4 (DPP4) inhibitors (sitagliptin, saxagliptin, linagliptin, etc), SGLT2 inhibitors (dapagliflozin,

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canagliflozin, etc.), GLP-1 agonists (exenatide, liraglutide, etc) and amylin analogue (pramlintide) (13).

Sulfonylurea antidiabetics reduce the blood sugar levels by inducing the release of insulin from beta cells of pancreas (14). They include first-generation drugs such as Tolbutamide, Chlorpropamide, etc and second-generation drugs like gliclazide, glipizide, glibenclamide, etc (15).

Nowadays, the use of complementary and alternative medicine (CAM) is common amongst patients with diabetes and other common chronic problems. It has been estimated that 9.8%–76.0% of general population tend to use CAM, globally (16). The CAM use found high in people such as women, those with literacy, those with employment, those with poor physical health, and those with diabetes or its comorbidities (17). Furthermore, it has been reported that the prevalence of CAM use in patients with diabetes is approximately 48% (18). The most frequently used CAM treatments among patients with diabetes include herbal medicines, nutritional advice, spiritual healing, massage, and meditation (19).

Herbal supplement use is getting popular among general population. A study from the United States found that approximately 35% of 26 157 participants used at least one herbal supplement (20). Up to 80% of population in developing countries use traditional herbal medicines as World Health Organization estimated it (21).

A study from Saudi Arabia comprising 228 patients with diabetes revealed that 24.6% of participants used herbal supplements (22) and an Iraqi study conducted among 884 diabetic patients found that 17.3% (153 respondents) of them used herbal supplements (23).

Drug interaction is defined as the interference of effects of one drug by the co-administered drugs, herbs, alcohol or tobacco smoke (24). The drug interaction leading to undesirable effects such as increased adverse effects or decreased beneficial effects, is termed 'adverse drug interaction'. The patients with diabetes are at heightened risk of adverse drug interactions, as they concomitantly use many medications to manage their comorbidities such as hypertension, dyslipidemia, heart diseases, depression, infections, etc, along with their antidiabetic medications (25). The probability of adverse drug interactions in diabetic patients is particularly high in patients who use sulfonylureas with herbal medicines. The present review is aimed to present the herbal drugs having interacting potentials with sulfonylurea antidiabetics.

Methods

The literature was searched in databases such as PubMed, Google Scholar, Science Direct, Directory of open access journals (DOAJ) and reference lists were searched using the keywords Drug interactions, Sulfonylureas, Pharmacodynamic interactions, Antidiabetic herbs, Pharmacokinetic interactions and CYP2C9.

Results

The herbal supplements taken by diabetic patients may interact with sulfonylureas either pharmacokinetically or pharmacodynamically. Sulfonylurea antidiabetics are metabolised primarily by cytochrome P450 2C9 (CYP2C9) enzyme (26) and by CYP3A4 enzyme to a lesser extent (27). Hence, the herbal drugs capable of modulating CYP enzymes may interact with sulfonylureas, pharmacokinetically (Table 1). As it was stated sulfonylureas are potent antidiabetic drugs and their concomitant use with certain herbs having antidiabetic activity may enhance the risk of hypoglycemia (Table 2).

St John's Wort (*Hypericum perforatum*)

St John's Wort is a herbal drug popularly used to treat depression. It can induce many CYP enzymes including CYP3A4 and CYP2C9 (28). The plasma concentrations of gliclazide decreased due to the concomitant use of St John's Wort, which could induce the CYP-mediated metabolism of gliclazide. It is recommended to monitor the signs of reduced hypoglycemic activity of sulfonylureas in patients with diabetes taking the combination of sulfonylureas and St John's Wort (29).

Ginkgo biloba

Ginkgo biloba may be useful to treat some neurological, psychological, and behavioral disorders.

The animal (30) and clinical (31) studies have identified that CYP2C9-mediated metabolism of tolbutamide

Table 1. Pharmacokinetic Herb – Sulfonylureas Interactions

Interacting Drugs	Mechanism of Interaction	Comments
St John's Wort (*Hypericum perforatum)*	St John's Wort may induce CYP-mediated metabolism of sulfonylureas and decrease their plasma concentrations.	Monitor the signs of reduced hypoglycemic activity of sulfonylureas in patients with diabetes taking the combination of sulfonylureas and St John's Wort (29).
Ginkgo biloba	*Ginkgo biloba* may decrease the plasma concentrations of sulfonylureas (31).	The hypoglycemic effect of sulfonylureas may be decreased.
Pomegranate (*Punica granatum*) Juice	Pomegranate Juice may inhibit CYP2C9-mediated metabolism of sulfonylureas.	Pomegranate Juice potentiate the hypoglycemic effect of tolbutamide (32).
Pineapple juice	The pineapple juice may inhibit the CYP2C9-mediated metabolism of sulfonylureas.	The plasma concentrations of sulfonylureas might be elevated by pineapple juice.

Table 2. Pharmacodynamic herb – sulfonylureas interactions

Interacting Drugs	Mechanism of Interaction	Comments
Bitter melon (Karela) (*Momordica charantia*)	Bitter melon may reduce blood sugar by exhibiting sulfonylurea like activity (35), improving glucose tolerance (36, 37), decreasing insulin resistance (38), increasing tissue glucose uptake (39, 40) or by increasing insulin sensitivity (41).	Additive reductions in blood glucose may result if sulfonylureas are used in patients consuming bitter melon regularly (43).
Fenugreek (*Trigonella foenum-graceum*)	Fenugreek may exert its hypoglycemic activity through improved insulin resistance in adipocytes (47) and liver (48), enhanced glucose uptake (49), increased activities of hepatic enzymes such as glucokinase and hexokinase (50), elevation of serum insulin levels (51) and increased insulin sensitivity (52).	Fenugreek use in patients taking sulfonylureas may further decrease the blood glucose levels (53, 54).
Cinnamon	Antihyperglycemic effect of Cinnamon may occur through insulin mimetic activity (59, 60), reduction of insulin resistance (61, 62), inhibition of pancreatic α-amylase and α-glucosidase enzymes (63), enhancement of glucose uptake (64), stimulation of glycogen synthesis (65), inhibition of gluconeogenesis (66) and delayed gastric emptying (67).	The dose of sulfonylureas may need to be adjusted if the patient is taking cinnamon concurrently (68).
Gymnema (*Gymnema sylvestre*)	Gymnema may reduce the glucose levels by delaying glucose absorption (74), enhancing insulin secretion (75-77), increasing glucose uptake in the liver, kidney and muscle (78) and inducing repair or regeneration of pancreatic beta cells (79, 80).	Concomitant use of sulfonylureas and Gymnema may result in potentiation of hypoglycemic effects (81, 82).
Ginseng	Ginseng may produce its antihyperglycemic activity by stimulating insulin production and preventing β cell loss (87-89), stimulating insulin release (90-93), improving insulin sensitivity (94-96), decreasing insulin resistance (97, 98), increasing glucose uptake (99-101), suppressing hepatic glucose production (102, 103), improving the regulation of plasma glucose and plasma insulin (104) and improving the expression of Peroxisome proliferator-activated receptors (PPARγ) (105, 106).	Ginseng may potentiate the hypoglycemic activity of sulfonylureas (107).
Ginger (*Zingiber officinale*)	Ginger may exhibit its antihyperglycemic activity through improvement of insulin resistance (111, 112), enhancement of glucose uptake (113, 114), increased insulin synthesis (115), decreased gluconeogenesis and glycogenolysis and increased glycogenesis (116) and inhibition of α-glucosidase and α-amylase enzymes (117).	The blood glucose levels should be monitored in patients taking sulfonylureas and ginger together, to avoid the occurrence of hypoglycemia (118).
Garlic (*Allium Sativum*)	Garlic may decrease the blood glucose levels through direct or indirect stimulation of insulin secretion (123,124), enhanced glucose utilization (125) and slowing down glucose absorption (126).	Caution should be applied in patients taking sulfonylureas and garlic together (127,128).
Aloe vera (*Aloe barbadensis* Miller*)*	*Aloe vera* may exert it's hypoglycemic activity by improving insulin resistance (135-137), stimulating the release of insulin (138), inhibiting pancreatic α-amylase activity (139), increasing glucose utilization and suppressing glucose production (140).	Aloe vera can potentiate the hypoglycemic effect of sulfonylureas (141).
Sesame oil [*Sesamum indicum***]**	Diabetes patients may prefer sesame oil as it reduces the detrimental effects of diabetes by improving glucose control, blood pressure, lipid levels and cardiac and renal health (149-152).	Sesame oil may improve hyperglycemia of patients taking sulfonylureas (153).
Andrographis paniculata	Andrographolide of *Andrographis paniculata* reduced the plasma glucose in streptozotocin-induced diabetic rats by increasing glucose utilization (154).	Use *Andrographis paniculata* (Andrographolide) with caution in patients taking sulfonylureas to avoid the risk of hypoglycemia (155).
Neem (*Azadirachta indica)*	*A. indica* found to decrease the blood glucose level by improving carbohydrate metabolism through the stimulation of the β-cells in streptozotocin-induced diabetic mice (157).	Concomitant use of aqueous extract of *A. indica* with gliclazide produced good control of blood glucose (158).

is induced significantly by *G. biloba* extract, resulting in decreased plasma concentrations and reduced hypoglycemic effect of tolbutamide.

Pomegranate (*Punica granatum*) juice

Pomegranate juice may inhibit CYP2C9 activity and increase the plasma concentration of tolbutamide resulting in potentiation of the hypoglycemic effect (32).

Pineapple juice

Pineapple juice contains bromelain as the principal component and it has been shown that CYP2C9 activity

is inhibited strongly by Pineapple juice in vitro (33). The pineapple juice may inhibit the CYP2C9-mediated metabolism of sulfonylureas and elevate their plasma concentrations due to its very strong CYP2C9 inhibitory activity, in vitro.

In the following section the possible interaction of sulfonylureas with medicinal plants which have antidiabetic activities are presented.

Bitter melon or bitter gourd (*Momordica charantia*)

Bitter melon (Karela) is a tropical and subtropical vegetable and it is used traditionally to treat diabetes, abdominal pain, jaundice, cough, respiratory diseases, skin diseases, wounds, ulcer, gout and rheumatism, etc (34). It is commonly included in Asian diet. Bitter melon may reduce blood sugar by exhibiting sulfonylurea like activity (35), improving glucose tolerance (36,37), decreasing insulin resistance (38), increasing tissue glucose uptake (39,40) or by increasing insulin sensitivity (41). The active principles, which may be responsible for the hypoglycemic activity of bitter melon, include polypeptide P, momordin, charantin and vicine (42).

Additive reductions in blood glucose may result if sulfonylureas are used in patients consuming bitter melon regularly. Potentiation of hypoglycemic activity of glibenclamide was also noted in patients taking bitter melon extract (43). Blood sugar should be monitored and the dosage adjustment of sulfonylureas may be necessary to avoid hypoglycemic complications.

Fenugreek (*Trigonella foenum-graceum*)

Fenugreek is a popular condiment and is largely produced in Indian subcontinent. Traditional uses of fenugreek include antidiabetic, analgesic, anti-inflammatory, anti-atherosclerotic, carminative, laxative, antispasmodic, anticancer, sexual stimulant, astringent, cardio tonic, antihypertensive, anti-triglyceridemic, lactation stimulant and oxytocic (44). Fenugreek contains constituents like carbohydrates, proteins, lipids, alkaloids, flavonoids, fibers, saponins, steroidal saponins, vitamins, minerals, etc (45). But, the hypoglycemic activity of fenugreek majorly determined by the active principles such as 4-hydroxyleucine, galactomannan rich fiber, and saponins (46). Fenugreek may exert its hypoglycemic activity through improved insulin resistance in adipocytes (47) and liver (48), enhanced glucose uptake (49), increased activities of hepatic enzymes such as glucokinase and hexokinase (50), elevation of serum insulin levels (51), and increased insulin sensitivity (52). Fenugreek use in patients taking sulfonylureas may further decrease the blood glucose levels (53,54).

Fenugreek seed extract exhibited synergistic effect on hypoglycemic potential of glibenclamide. Caution is advised in patients taking an antidiabetic drug and a herb like Fenugreek concomitantly, to prevent hypoglycemic complications (55).

Cinnamon

Cinnamon is an inner bark of the trees of the genus Cinnamomum. Cinnamon is commonly used as a spice in many countries. There are many species of cinnamon available all around the world, which includes True cinnamon or Sri Lanka cinnamon or *Ceylon cinnamon* (*Cinnamomum verum* or *Cinnamomum zeylanicum),* Chinese cinnamon or cassia cinnamon *(Cinnamomum cassia),* Indonesian cinnamon (*Cinnamomum burmannii),* Vietnamese cinnamon or Saigon cinnamon (*Cinnamomum loureiroi)*, etc (56). Many studies have confirmed that Cinnamon possesses antidiabetic, cholesterol-lowering, antioxidant, antitumor, anti-inflammatory, antimicrobial, cardio-vascular and immunomodulatory effects (57). Active chemical constituents of cinnamon include cinnamaldehyde, coumarins, essential oils, procyanidins, etc (58). Antihyperglycemic effect of Cinnamon may occur through insulin mimetic activity (59,60), reduction of insulin resistance (61,62), inhibition of pancreatic α-amylase and α-glucosidase enzymes (63), enhancement of glucose uptake (64), stimulation of glycogen synthesis (65), inhibition of gluconeogenesis (66) and delayed gastric emptying (67).

Addition of cinnamon, improved the glucose control and lipid levels in patients with poorly controlled type 2 diabetes taking sulfonylureas (68). To prevent hypoglycemia, the dose of sulfonylureas may need to be adjusted if the patient is taking cinnamon concurrently.

Gymnema (*Gymnema sylvestre*)

Gymnema is a herb found vastly in India and Srilanka. Traditionally, *Gymnema* is used to treat diabetes, dyspepsia, constipation, jaundice, haemorrhoids, cardiopathy, asthma, bronchitis and leukoderma. In addition, it has been found to contain antidiabetic, antiobesity, hypolipidaemic, antimicrobial, antioxidant, diuretic, antihelmentic and anti-inflammatory properties (69-71). Active phytoconstituents of *Gymnema* include triterpene saponins (gymnemic acids and gymnemasaponins, gymnemasides), flavones, anthraquinones, resins, alkaloids, etc (72,73). Gymnemic acids of *Gymnema* is responsible for the antidiabetic activity. *Gymnema* may reduce the glucose levels by delaying glucose absorption (74), enhancing insulin secretion (75-77), increasing glucose uptake in the liver, kidney and muscle (78) and inducing repair or regeneration of pancreatic beta cells (79,80).

Significant reduction of fasting blood glucose and lipid levels has been noted in patients with type 2 diabetes receiving sulfonylurea treatment along with 400 mg of *Gymnema* daily for 18 to 20 months (55, 79). Concomitant use of sulfonylureas and Gymnema may result in potentiation of hypoglycemic effects (81,82).

Ginseng

Ginseng root is a popular herb and there are many varieties of ginseng available including Asian ginseng or Korean ginseng (*Panax ginseng)* and American ginseng (*Panax quinquefolius)* (83). Ginseng is used in traditional Chinese medicine (TCM) to treat diabetes, impotence, anorexia, insomnia, palpitation, shortness of breath and hemorrhage (84). The active principles found in ginseng include ginsenosides, polysaccharides, polyynes, flavonoids, peptides, polyacetylenic alcohols and volatile oils (85). The most pharmacologically active constituents of ginseng are ginsenosides and they possess antioxidant, antiinflammatory, anticarcinogenic and immunostimulant properties (86). Ginseng may produce its antihyperglycemic activity by stimulating insulin production and preventing β cell loss (87-89), stimulating insulin release (90-93), improving insulin sensitivity (94-96), decreasing insulin resistance (97,98), increasing glucose uptake (99-101), suppressing hepatic glucose production (102,103), improving the regulation of plasma glucose and plasma insulin (104) and improving the expression of peroxisome proliferator-activated receptors (PPARγ) (105, 106). In sum, ginseng may potentiate the hypoglycemic activity of sulfonylureas (107).

Ginger (*Zingiber officinale*)

Ginger root is used as a cooking spice in foods. Traditionally ginger is used to treat various conditions including diabetes, asthma, stroke, constipation, rheumatism, nervous diseases, gingivitis, toothache, etc (108). Phytochemical studies of ginger revealed that it contained terpenes (Zingiberene, β-bisabolene, α-farnesene, β-sesquiphellandrene, and α-curcumene), phenolic compounds (Gingerol, paradols, and shogaol), amino acids, raw fiber, ash, protein, phytosterols, vitamins and minerals (109,110). Ginger may exhibit its antihyperglycemic activity through improvement of insulin resistance (111,112), enhancement of glucose uptake (113,114), increased insulin synthesis (115), decreased gluconeogenesis and glycogenolysis and increased glycogenesis (116) and inhibition of α-glucosidase and α-amylase enzymes (117).

Concomitant administration of ginger extract (25 or 50 mg/kg) and glibenclamide (5 mg/kg) in streptozotocin (STZ)-induced diabetic rats, decreased the non-fasting blood glucose level significantly. The blood glucose levels should be monitored in patients taking sulfonylureas and ginger together, to avoid the occurrence of hypoglycemia (118).

Garlic (*Allium sativum*)

Garlic is a natural medicinal plant and is used as a flavoring substance in food preparations. Garlic found helpful to lower blood sugar, reduce cholesterol levels, prevent cardiovascular diseases, enhance the immune system and regulate blood pressure. It is effective against bacterial, viral, fungal and parasitic infections (119). The phytochemicals of garlic include sulfur compounds (allicin, alliin and agoene), volatile oils, enzymes (allinase, peroxidase and miracynase), carbohydrates (sucrose and glucose), minerals (selenium), amino acids (cysteine, glutamine, isoleucine and methionine), bioflavonoids (quercetin and cyanidin, allistatin I and allistatin II) and vitamins (C, E, A, niacin, B1 and B2 and betacarotene (120). Sulphur compounds of garlic are linked to the hypoglycemic activity (121,122). Garlic may decrease the blood glucose levels through direct or indirect stimulation of insulin secretion (123,124), enhanced glucose utilization (125) and reduction of glucose absorption (126).

Greater hypoglycemic activity was noted in streptozotocin-induced diabetic rats receiving the combination of garlic extract (500 mg/kg) and glibenclamide (0.25 or 0.5 mg/kg) than either of the drug given alone (127). Caution should be applied in patients taking sulfonylureas and garlic together (127,128).

Aloe vera (*Aloe barbadensis* Miller)

Aloe vera is traditionally used to treat various conditions in many countries. Active components of *Aloe vera* include anthraquinones (aloin, barbaloin, isobarbaloin, anthranol, etc), hormones (auxins and gibberellins), enzymes (cyclooxygenase, oxidase, amylase, catalase, lipase, alkaline phosphatase, carboxypeptidase), vitamins (B1, B2, B6, choline, folic acid, C, α-tocopherol, β-carotene), minerals (calcium, sodium, chlorine, manganese, zinc, chromium, etc), sugars (cellulose, glucose, mannose, etc), amino acids (lysine, threonine, valine, leucine, isoleucine, phenylalanine, methionine) (129-131). *Aloe vera* was found to possess therapeutic properties such as antidiabetic, antibacterial, antiviral, antifungal, anti-inflammatory, anticancer, antioxidant, wound healing and immunostimulation activities (132-134). *Aloe vera* may exert its hypoglycemic activity by improving insulin resistance (135-137), stimulating the release of insulin (138), inhibiting pancreatic α-amylase activity (139), increasing glucose utilization and suppressing glucose production (140).

Significant improvement in blood glucose level and lipid levels was seen in diabetic patients taking *Aloe vera* juice (15 mL two times daily) and glibenclamide (10 mg daily) concurrently (141).

Sesame (*Sesamum indicum*) oil

Sesame oil is widely used for cooking in South India and other parts of the world. Sesame oil is composed of lignans (sesamin, sesamolin), minerals, vitamins, phytosterols, unsaturated fatty acids (linoleic acid, oleic acid, etc) and tocopherols (142-144). Many studies have shown that sesame oil has antioxidant, antihypertensive, antihyperlipidemic, antihyperglycemic, anticarcinogenic and immunoregulatory activities (145-148). Diabetes patients may prefer sesame oil as it reduces the detrimental

effects of diabetes by improving glucose control, blood pressure, lipid levels and cardiac and renal health (149-152).

The type 2 diabetes patients taking the combination of sesame oil (~35 g oil/day used in cooking or salad preparation) and glibenclamide (5 mg daily) showed a greater anti-hyperglycaemic effect (153).

Andrographis paniculata

Andrographis paniculata is a medicinal plant used traditionally to treat various illnesses like infections, liver problems, diabetes, etc. The principal constituent of *A. paniculata* is androdrographolide, which has been shown to reduce the plasma glucose in streptozotocin-induced diabetic rats by increasing glucose utilization (154).

The hypoglycemic effect of glyburide enhanced considerably by the coadministration with androdrographolide. The herbal preparations containing *A. paniculata* (androdrographolide) should be used in patients taking sulfonylureas with special attention to avoid the risk of hypoglycemia (155).

Neem (*Azadirachta indica*)

Azadirachta indica is a traditionally used medicinal plant, which has anti-inflammatory, immunostimulant and hypoglycemic activities (156). A. *indica* found to decrease the blood glucose level by improving carbohydrate metabolism through the stimulation of the β-cells in streptozotocin-induced diabetic mice (157). Concomitant use of aqueous extract of *A. indica* with gliclazide produced good control of blood glucose (158).

Conclusion

Use of herbal medicines to treat diabetes is getting popular around the world. The herbs like St. John's wort and Gingko biloba induce CYP2C9-mediated metabolism of sulfonylureas while the fruit juices like Pomegranate juice and Pineapple juice inhibit their metabolism. In addition, the antidiabetic herbal supplements such as bitter melon, fenugreek, cinnamon, Gymnema, ginseng, ginger, garlic, *Aloe vera*, sesame, andrographis paniculata and neem potentiate the hypoglycemic activity of sulfonylureas pharmacodynamically. The prescribers and the pharmacists should be aware of the herbs interacting with sulfonylureas to prevent adverse outcomes.

Authors' contributions

NMPM and RB conceived the presented idea. NMPM drafted the manuscript. RB reviewed it. All read and confirmed its publication.

Conflict of interests

None.

Ethical considerations

Ethical issues including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy, have been carefully observed by authors.

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