Chapter

Antidiabetic Potential of Plants Used in Bulgarian Folk Medicine and Traditional Diet

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Abstract

The idea of this chapter is that currently available antidiabetic drugs specifically target several points of the T2D pathophysiology but they do not cover all aspects of the disease. In addition, many adverse effects of synthetic antidiabetic agents have been reported. The suggested manuscript is an overview of the available scientific literature focused on antiobesity and antidiabetic potential of selected 42 medicinal and edible plants of the Bulgarian flora. Most of the reports reveal the effect of extracts or their active components on specific biochemical mechanisms. Mechanistic data about hypoglycemic and hypolipidemic action are presented for some of the plants. An essential part of this review is dedicated to the target mechanisms behind the effects of the selected plant species. The authors hope that this review will serve as a starting point for future investigations with a contribution to the prevention and therapy of diabetes.

Keywords: medicinal plants, diabetes, folk medicine, traditional diet

1. Introduction

Diabetes is an endocrine disease related to impaired glucose metabolism due to either impaired insulin secretion or decreased sensitivity to its function, classified, respectively, as type 1 diabetes (T1D) and type 2 diabetes (T2D). Over time, chronic hyperglycemia can cause secondary micro- and macrovascular complications affecting the functions of the eyes, kidneys, peripheral nerves, and arteries. According to recent alarming data, the number of adults living with diabetes has almost quadrupled since 1980 to 2014. This dramatic rise is largely due to the number of T2D sufferers [1].

Although some of the characteristics of the modern lifestyle (obesity, stress, low physical activity) are considered to be risk factors with regard to the occurrence of diabetes, it should be noted that cases of the disease are described in written sources dating back to 3500 years [2–4]. Also, records exist from ancient Egypt, India, and Persia, indicating a long history of medicinal use of plants for treatment of conditions associated with diabetes [5]. Historical and archeological sources indicate that Thracians, the most ancient tribes on the territory of Bulgaria, were familiar with the healing power of the plants [6]. Over the years, empirical data about healing properties of plants used in Bulgarian folk medicine and traditional nutrition have been collected in several reference books [7–10]. Although plants have been used to treat diabetes for centuries, the number of species with completely clarified antidiabetic mechanisms of action is still limited.

No.	Plant	Common name	Used parts	References
1	*Achillea millefolium* L. (Asteraceae)	White yarrow	Aerial parts	[13–20]
2	*Agrimonia eupatoria* L. (Rosaceae)	Agrimony	Aerial parts	[21–31]
3	*Alchemilla vulgaris* L. (Rosaceae)	Lady's Mantle	Stalk	[21, 32, 33]
4	*Arctium lappa* L. (Asteraceae)	Burdock	Root	[21, 34–36]
5	*Arctostaphylos uva-ursi* L. (Ericaceae)	Bearberry	Leaves	[37, 38]
6	*Asparagus officinalis* L. (Liliaceae)	Sparrow grass	Stalk	[39–41]
7	*Berberis vulgaris* L. (Berberidaceae)	Barberry	Fruits	[42–44]
8	*Betula* sp. (Betulaceae)	Birch	Leaves	[45, 46]
9	*Cichorium intybus* L. (Asteraceae)	Blue daisy, blue dandelion	Stalk, root	[13, 14, 21, 47]
10	*Cotinus coggygria* Scop. (Anacardiaceae)	Smoke tree, sumach	Leaves	[25, 48]
11	*Cydonia vulgaris* Pers. (Rosaceae)	Quince	Leaves	[49–51]
12	*Foeniculum vulgare* Mill. (Apiaceae)	Dill	Fruits	[52–54]
13	*Fragaria vesca complex* (Rosaceae)	Wild strawberry	Leaves	[33, 55, 56]
14	*Galega officinalis* L. (Fabaceae)	Goat's rue	Stalk	[21, 57–59]
15	*Hypericum perforatum* L. (Hypericaceae)	St. John's wort	Stalk	[25, 60, 61]
16	*Juglans regia* L. (Juglandaceae)	Walnut	Leaves	[62–69]
17	*Juniperus communis* L. (Cupressaceae)	Juniper	Fruits	[13, 14, 21, 31]
18	*Lavandula angustifolia* Mill. (Liliaceae)	Lavender	Flower	[21, 25, 70, 71]
19	*Melissa officinalis* L. (Liliaceae)	Melissa, lemon balm	Stalk	[25, 58, 71, 72]
20	*Mentha piperita* L. (Liliaceae)	Mint	Leaves	[33, 71]
21	*Morus nigra* L. (Moraceae)	Mulberry	Leaves, fruits, root bark, heartwood	[13, 14], 76–82
22	*Ocimum basilicum* L. (Liliaceae)	Basil	Leaves	[73–75]
23	*Ononis spinosa* L. (Lamiaceae)	Spiny restharrow	Root	[62]
24	*Origanum vulgare* L. (Liliaceae)	Marjoram	Stalk	[25, 83–85]
25	*Pelargonium sp.* (Geraniaceae)	Pelargonium	Leaves	[86, 87]
26	*Phaseolus vulgaris* L. (Fabaceae)	Bean	Pods	[13, 14, 21, 88–91]
27	*Plantago major* L. (Plantaginaceae)	Broadleaf plantain	Leaves	[62]
28	*Polygonum aviculare* L. (Polygonaceae)	Prostrate knotweed, birdweed, pigweed	Stalk	[26]
29	*Rheum officinale* Baill. (Polygonaceae)	Rhubarb	Root	[92, 93]

No.	Plant	Common name	Used parts	References
30	*Rosa canina* L. (Rosaceae)	Rose hip	Fruits	[55, 94–96]
31	*Rosa damascen*a *auct.* non-Mill. (Rosaceae)	Oil rose	Flower	[97–98]
32	*Rubus sp.* diversae	Бlackberry	Leaves	[21, 25, 100, 101]
33	*Salvia officinalis* L. (Liliaceae)	Garden sage	Leaves	[19, 47, 102–106]
34	*Sambucus ebulus* L. (Caprifoliaceae)	Dwarf elderberry	Fruits	[33, 107–110]
35	*Sambucus nigra* L. (Caprifoliaceae)	European black elderberry	Flower	[34, 111–113]
36	*Taraxacum officinale* Wigg. (Asteraceae)	Dandelion	Root stalk	[19, 21, 34, 81, 114]
37	*Thymus* sp. diversae (Liliaceae)	Thyme	Stalk	[19, 77]
38	*Tilia platyphyllos* Scop. (Tiliaceae)	Lime tree	Flower	[37, 115]
39	*Urtica dioica* L. (Urticaceae)	Nettle	Stalk	[34, 67, 116–120]
40	*Vaccinium myrtillus* L. (Ericaceae)	Blueberry	Leaves and fruits	[13, 14, 21, 81]
41	*Veronica officinalis* L. (Scrophulariaceae)	Veronica, speedwell, Paul's betony	Stalk	[121, 122]
42	*Zea mays* L. (Poaceae)	Corn	Silk	[21, 123]

Table 1.
References in support of potentially antidiabetic properties of 42 selected plants.

Currently available antidiabetic drugs could specifically target several points of the T2D pathophysiology, but they do not cover all aspects of the disease [11, 12]. In addition, many adverse effects of synthetic antidiabetic agents have been reported [11].

Therefore, it is not surprising that in recent years, the scientific interest is focused on identifying naturally derived compounds and preparations with hope to address more aspects of the disease without undesirable side effects.

This chapter is an overview of the available scientific literature focused on antiobesity and antidiabetic potential of selected 42 medicinal and edible plants of the Bulgarian flora. Most of the reports reveal the effect of extracts or their active components on specific biochemical mechanisms. Mechanistic data for hypoglycemic and hypolipidemic action are presented for some of the plants (references summarized in **Table 1**). An essential part of this review is dedicated to the target mechanisms behind the effects of the selected plant species.

Without claiming exhaustiveness, the authors hope that this review will serve as a starting point for future investigations with a contribution to the prevention and therapy of diabetes.

2. Effects of plants and plant-derived compounds on glucose homeostasis

2.1 Inhibition of digestive enzymes and glucose absorption in the intestine

Carbohydrates are an essential part of the human diet and are the main energy source of the body. Starch, sucrose, lactose, and glycogen are the main utilizable carbohydrates in human diet. After the action of salivary and pancreatic α-amylase, the digestion products of starch and glycogen along with disaccharides are further digested in the small intestine epithelium, where the membrane-bound enzyme α-glucosidase, as well as various disaccharidases (saccharase, maltase, lactase), catalyze the release of glucose, fructose, and galactose. Monosaccharides are absorbed through the walls of the small intestine and reach the liver by the portal vein.

Inhibition of digestive enzymes is one possible approach to control early-stage hyperglycemia. Inhibition of α-amylase and α-glucosidase can significantly delay the increase in glucose concentration in the postprandial phase [124–127].

For a significant part of the plants presented in **Table 1**, data on the inhibitory effect of their extracts or active components on digestive enzymes in different experimental approaches were reported (**Table 2**). In vitro studies have found that aqueous extracts of basil and walnut leaves exert an inhibitory effect on α-amylase and α-glucosidase as well as on some disaccharidases without affecting insulin secretion and glucose transport proteins [63, 79]. Both studies suggest that polyphenols play a major role in the observed effects, as an extremely rich content of these active compounds in the two extracts is found. Another study [128] demonstrated a strong inhibitory activity of walnuts on the activity of α-amylase and disaccharidases.

Except aqueous extract of thyme, the extracted essential oil of the plant also exhibits an inhibitory effect on the amylase and glucosidase; Paddy et al. [19] and Pongpiriyadacha et al. [46] found that birch extract significantly reduced blood glucose levels after oral administration of sucrose to rats, a result demonstrating the inhibitory action of the extract on α-glucosidase. The same extract in an in vitro study had a concentration-dependent inhibitory effect on α-glucosidase, saccharase, and maltase.

2.2 Effects on glucose homeostasis in the liver

The liver has an essential role in maintenance of glucose homeostasis by controlling the utilization of excess glucose after meal for glycogen synthesis or secretion of free glucose into the circulation through glycogenolysis and gluconeogenesis (GNG) in fasting periods. Insulin and glucagon have a major regulatory role in the activity of these processes. In the periods when the nutrients do not enter the body, all the glucose coming into the circulation is delivered by the liver [129]. Upon food intake, increased glucose levels stimulate secretion of insulin, which has an inhibitory effect on hepatic mechanisms delivering free glucose.

In diabetic patients, this regulation is impaired, and even an increased activity of the key enzymes of gluconeogenesis and glycogenolysis is detected [130, 131].

Galega officinalis has been used from ancient times to alleviate polyuria in diabetic patients. Its active ingredients guanidine and gelagine have been shown to inhibit the enzyme fructose-1,6-bisphosphatase and glucose-6-phosphatase (**Table 2**).

Fructose-1,6-bisphosphatase is a rate-limiting enzyme in GNG, and its activity has been reported to be pathologically elevated in experimental models of insulin resistance (IR) and obesity [132]. Therefore, inhibition of the enzyme could be a promising target to overcome the chronic hyperglycemia and to maintain normoglycemic status during fasting periods. The search for new GNG inhibitors of natural origin may be of great importance in the control of diabetes, especially for patients intolerant to synthetic therapeutics [11].

Glucose-6-phosphatase is a key enzyme in GNG and glycogenolysis, catalyzing the last step—release of free glucose from the liver.

Several plants from our list are described to exert their hypoglycemic action by inhibiting enzymes from GNG (**Table 2**). According to folk medicine, *Melissa* sp. has

Metabolic pathway/ mechanism	Effects on molecular targets	Plant No.	Type of studies
Carbohydrate digestion and absorption	↓ α-amylase	1, 3, 6, 8, 22, 26, 30, 31, 33, 36, 37, 39	Spectrophotometrical assessment of enzyme inhibition; STZ-induced diabetes; kinetics of enzyme inhibition
	↓ α-glucosidase	1, 6, 8, 22, 26, 30, 31, 33, 36, 37	Spectrophotometrical assessment of enzyme inhibition; glucose oxidase-based method
	↓ Disaccharidases	16, 22	Intestinal sucrase and maltase in rats with alloxan-induced diabetes
	↓ Glucose absorption	1, 17, 33, 36, 37	Intestinal cell cultures; diabetic rodents
GNG	PEPCK	16, 19, 21	Gene expression in hepatocytes of diabetic rodents
	Fructose-1,6-bisphosphatase	14	Experimental and clinical studies with metformin
	Glucose-6 phosphatase	14, 19	Gene expression in hepatocytes of diabetic rodents; experimental and clinical studies with metformin
Glycogen synthesis	Glucokinase	16, 19	Gene expression in hepatocytes of diabetic rodents
	Glycogen synthase	2, 6, 35	STZ-induced diabetes in rats; mice muscle cell cultures
Polyol pathway	Aldose reductase	5, 24, 42	Diabetic rodents; in vitro enzyme activity in rats lences
Glucose uptake in IDTs	GLUT-4 translocation	1, 16, 18, 19, 20,, 26, 33, 36, 37, 41	Glucose uptake in C2C12 myotubes; gene expression in 3T3-L1 cell culture
Insulin secretion	SUR1 and Ca^{2+} channels	1, 2, 4, 6, 9, 16, 28	[Ca^{2+}] and [insulin] in pancreatic beta cells
Lipid metabolism	↓ TAG	1, 2, 13, 16, 26, 30, 34	Rats with alloxan- or STZ-induced diabetes; human intervention studies 3T3-L1 cell cultures
	↓ VLDL	1	Rats with alloxan- or STZ-induced diabetes
	↓ HMG-CoA reductase	4, 9, 20, 22, 31, 39	Macrophage and 3T3-L1 cell cultures
	↓ Total cholesterol	1, 2, 16, 33, 34	Rats with alloxan- or STZ-induced diabetes; human intervention studies
	↓ LDL	1, 2, 34	Rats with alloxan- or STZ-induced diabetes; human intervention studies
	↑ HDL	16, 34, 36	Rats with alloxan- or STZ-induced diabetes; human intervention studies; cholesterol fed rabbits
	↑ HDL/LDL ratio	2, 34	Human intervention studies

Plant numbers are in the order as they are listed in ***Table 1****.*

Table 2.
Mechanisms of action of selected plants in respect of their antidiabetic potential; ↑-activation, ↓-inhibition.

pronounced spasmolytic and antibacterial action and a slight anxiolytic effect [7]. Scientific data from recent years reveal the antidiabetic potential of the plant ([72]. It was demonstrated that chronic administration of neral and geranial essential oils to db/db mice had significant hypoglycemic effect, due to their stimulatory and, respectively, inhibitory effects on the gene expression of glucokinase and glucose-6-phosphatase.

The enzyme glucokinase, also called the "glucose sensor," has a key role in the pancreas and liver to maintain glucose homeostasis. Due to the fact that the enzyme has a high Km value for glucose, its role is to provide an excess of glucose (by phosphorylation to glucose-6-phosphate) to activate insulin secretion and glycogen synthesis. The search for active compounds that can stimulate the enzyme is a relatively new concept in the pharmacological approaches to diabetes treatment [11], and probably the role of medicinal plants as sources of such activators is yet to be explored.

The key enzyme for glycogen synthesis is glycogen synthase. *Agrimonia eupatoria* L., *Asparagus officinalis* L., and *Sambucus nigra* L. have shown a stimulating effect on the enzyme activity, but the mechanisms behind this effect remain unclear. Treatment with agrimony and sparrow grass extracts has resulted in increased amount of glycogen in the muscles and liver of rats with streptozotocin-induced diabetes [23, 39]. Elderberry aqueous extract applied to isolated mouse muscle cells stimulated both glucose transport and oxidation as well as glycogen synthesis [111]. Similarly, in cells and animal studies, it was found that preparations and active compounds from *Morus* sp. have inhibitory effects on gene expression of all regulatory GNG enzymes, including phosphoenolpyruvate carboxykinase (PEPCK) [133, 134].

2.3 Inhibition of polyol pathway of glucose metabolism

The most serious problems resulting from diabetes mellitus are the complications due to increased blood glucose levels.

The body has several options to metabolize the excess glucose. Among them, the polyol pathway is of utmost importance for the development of diabetic complications. Catalyzed by the aldose reductase enzyme, glucose is converted to sorbitol, an osmotically active metabolite which accumulates and damages the cells [135]. It has been shown that inhibition of aldose reductase is preventive against the development of micro- and macrovascular diabetic complications [136, 137].

For three of the selected medicinal plants, data exist about their inhibitory effect on aldose reductase (**Table 2**). Treatment of diabetic mice with ursolic acid isolated from the bearberry resulted in a reduction in fructose and sorbitol levels in the kidneys [38]. Active components of oregano (caffeic and rosmarinic acid) and of maize hair (hirsutrin) have proven in their in vitro inhibitory action on aldose reductase activity in rat lenses [83, 123].

Research on potential enzyme inhibitors has so far not led to the development of therapeutics of general usage [138]. Although scarce, data on such activity of medicinal plants is promising in future quests for such a therapeutic approach.

2.4 Effects of glucose transport in insulin-dependent tissues

Insulin modulates several metabolic pathways by activating the phosphatidylinositol-3-kinase (PI3K) cascade, including intracellular translocation of the GLUT-4 transport protein for glucose in skeletal and adipose tissues. In diabetes, the transfer of GLUT-4 towards plasma membrane cannot be accomplished.

The hypoglycemic properties of some medicinal plants are due to the ability of their active components to promote the translocation of GLUT-4 to the plasma membrane, resulting in a decrease in blood glucose concentration [20, 90, 106, 139].

Hypoglycemic potential based on this mechanism has been reported primarily for essential oils of lavender, lemon balm, and mint [71, 72]. Luteolin, the flavan derived from *Veronica officinalis*, was shown to activate both the expression and translocation of the glucose transport protein [140].

2.5 Hypoglycemic activity of plants: putative mechanisms

Much of the data with regards to the antidiabetic activity of the plants were obtained using models of pharmacologically induced diabetes in experimental animals. The most commonly used diabetes-inducing agents are streptozotocin (STZ) and alloxan [141]. Both compounds have destructive effects on pancreatic β cells by different mechanisms. STZ enters the β cells through the transport protein GLUT-2 and damages DNA, resulting in overexpression of DNA repair systems and thus leading to depletion of cell stores of ATP and oxidized nicotinamide dinucleotide (NAD+) [142, 143]; alloxan, transported by GLUT-2, depletes the thiol groups in the cells, establishing a permanent redox cycle with the dialuric acid (its reduced form). This process leads to the accumulation of ROS and hence to the destruction of β cells, which in general have very limited store of endogenous antioxidants [144].

The models of in vivo induced diabetes are informative in terms of the hypoglycemic and insulin-like effects of plant extracts. For example, such was the effect of the aqueous oregano extract applied over a period of several weeks to rats with STZ-induced diabetes. In this study, the established potential of the extract to lower blood sugar and glycated hemoglobin was comparable to that of the antidiabetic drug glibenclamide [84]. In another similar in vivo study, the plant extract exhibited an insulin-like effect normalizing blood glucose levels without affecting plasma basal insulin levels [145]. Similar data was also obtained about black mulberry leaf extract [74]. However, in addition to the hypoglycemic effect, an increase in the insulin levels was reported, which may be attributed to the protective and possibly stimulatory action of the plant on β cells' function. Data on the antidiabetic properties of *Phaseolus vulgaris* exist in folk medicine of different ethnic groups [146]. At present, many scientific studies confirm the hypoglycemic and hypolipidemic potential of the plant (predominantly of the pod extract), both in experimentally induced diabetes and in human intervention studies [147–149]. *Vaccinium myrtillus* fruits had beneficial effect on obese subjects in a 6-week intervention study as measured by improved insulin sensitivity, inflammatory biomarker levels, and lipid profile [150]. *Zea mays* hair extracts, as recommended by folk medicine as an antidiabetic remedy, was shown to reduce blood sugar and glycated hemoglobin levels, to stimulate β cells' function and increase serum insulin levels in an experimental model of diabetes [151, 152]. Hypoglycemic and insulin-like effects have also been reported for *Taraxacum officinale* roots, for fruits and flowers of *Sambucus nigra*, stalks of *Alchemilla vulgaris* and *Achillea millefolium*, roots from *Arctium lappa* and *Urtica dioica*, *Cydonia vulgaris* leaves, and other plants presented in **Table 1**.

3. Effects of plants on insulin secretion

There are two mechanisms by which medicinal plants or their active components possibly stimulate insulin secretion [153]:

- Plant active compounds bind to sulfonylurea binding site 1 (SUR1) of K^+-ATP channels resulting in channel closure and membrane depolarization.

- Direct activation of Ca^{2+} channels.

Sulfonylurea derivatives, such as glibenclamide, are applied for treatment of T2D to stimulate translocation of insulin-containing secretory granules to plasma membrane and exocytosis of insulin in the extracellular matrix [11].

Medicinal plants with an effect on insulin secretion are presented in **Table 2**.

It should be noted that according to most of the studies, the stimulatory activity of medicinal plants on insulin secretion is attributed to their antioxidative potential and ability to prevent SZT- and alloxan-induced beta cell injury in experimental models of diabetes.

4. Plants that affect lipid metabolism

Defined as abnormal accumulation of adipose tissue, obesity is a major health problem worldwide [154]. As a condition that accompanies obesity, dyslipidemia is believed to be a basic factor for the development of obesity-related diseases such as T2D, cardiovascular diseases (CVD), and atherosclerosis [155]. Dyslipidemia is characterized by increased triacylglycerol (TAG) and total cholesterol levels and unfavorable changes in HDL-/LDL-cholesterol ratio [156, 157].

Many plants that are considered to have antidiabetic potential have beneficial effects on the lipid profile in addition to their hypoglycemic activities [158, 159]. These properties are attributed to their naturally occurring secondary metabolites, such as bioflavonoides.

Anthocyanin extracts and anthocyanin-rich diet can improve the parameters of lipid profile and therefore are considered to have anti-obesity and anti-atherogenic effects in humans and in rodents [160–164].

Sambucus ebulus (dwarf elderberry) is a plant widely used in Bulgarian folk medicine in various pathological conditions. Its fruits are rich in anthocyanins. Studies report that anthocyanin extracts can reduce body mass and adipose tissue volume in rats fed with high-fat and high-fructose diet [160, 165–167]. There are reports describing the also hypoglycemic activity of the *S. ebulus* fruits in rats on high-fat and high-fructose diet [168, 169].

A 30-day human intervention study with *S. ebulus* fruit tea decreased significantly TAG, total cholesterol, and LDL-cholesterol levels. Slight increase of HDL and significant increase in HDL/LDL ratio were found ([110].

Low HDL levels are recognized as an independent risk factor for the development of cardiovascular diseases [170]. Inhibition of cholesteryl ester transfer protein (CETP) is a probable cause for the increased HDL-cholesterol levels, and LDL-cholesterol levels decrease upon anthocyanin treatment [171]. Anthocyanins can decrease quantity and the activity of CETP in plasma of dyslipidemic patients [161].

The scientific data cited above are in support to the folk medicine reports about the healing properties of *S. ebulus* fruit preparations.

Likewise, lipid profile improving properties have been reported for *Agrimonia eupatoria* (agrimony). Its effect on lipid profile was estimated in our study in a model of metabolic disturbances in rats on high-fructose diet. Intake of 40% aqueous-ethanol extract prevented fat accumulation in the liver and adipose tissue and normalized levels of serum lipids [167].

In addition, we performed a human intervention study with 30-day agrimony tea consumption. As a result, increased levels of HDL cholesterol were established, and LDL-cholesterol levels remained unchanged at the same time [29]. These results reveal good potential of agrimony to improve lipid profile, which is important in prophylaxis of CVD and diabetes.

It can be assumed that polyphenols play a role in the mechanisms by which the plant manifests its effects. It is known that diet rich in polyphenols may improve lipid profile in individuals with normal or compromised health status [172, 173]. Polyphenol preparations and polyphenol-rich extracts have also the potential to improve lipid profile [174–177]. As it was already mentioned, *S. ebulus* fruits are a rich source of polyphenols and especially of anthocyanins [33, 108]. Also, it was found that the aqueous and aqueous alcoholic extracts of agrimony have a high polyphenol content [25, 178], although their exact polyphenol composition has not yet been identified. Polyphenols have limited bioavailability; however, many of the products of their intestinal metabolism overcome the intestinal barrier and reach the tissues where they exert their biological effects [179].

Some of the selected plants (**Table 1**) can exert their effects by inhibiting the activity of the rate-limiting enzyme in cholesterol synthesis—HMG-CoA reductase [99]. Cholesterol is the most abundant sterol in the human body and is essential for the normal functioning of the cells. Cholesterol homeostasis is of great importance for the health status. Apart from being a risk factor for atherosclerosis, increased plasma cholesterol levels are often an accompanying parameter of the metabolic disturbances, such as diabetes. Despite being applied for decades, HMG-CoA reductase inhibitors have adverse and unwanted effects, such as myopathy, liver insufficiency, etc. [99].

Even more, in a case of strictly controlled LDL-cholesterol levels by statins, not always TAG and HDL-cholesterol levels are sensitive to the therapy, and there is still a chance that CVD risk would remain high [180]. Interventions with *S. ebulus* and *A. eupatoria* tea resulted in significantly increased HDL/LDL ratio; beneficial effects of these plants on plasma TAG and total cholesterol levels were established, so it is likely that the plants improve all parameters of the lipid profile. This makes them promising sources of active compounds with a potential to prevent and supplement the therapy of T2D and CVD.

In addition to the above, scientific data about the beneficial effects of rosehip, strawberries, and raspberries on lipid metabolism and inflammation exist (**Table 1**). These plants are rich in the glycoside flavonoid tiliroside, which was shown to inhibit postprandial inflammation, to play a role in the prevention of obesity, hyperinsulinemia, and hyperlipidemia. Its action is associated with elevated levels of adiponectin and also facilitated fatty acids oxidation in the liver and skeletal muscles [181]. Strawberry anthocyanin pelargonidin sulfate and pelargonidin-3-O-glycoside reduced postprandial inflammation and increased insulin sensitivity in overweight individuals [56]. Polyphenols extracted from strawberry decreased postprandial LDL oxidation and enhanced lipid metabolism in a high-fat intervention with overweight individuals with hyperlipidemia [182]. Six of the plants listed in **Table 1** (*Arctium lappa*, *Cichorium intybus, Mentha piperita, Ocimum basilicum, Rosa damascen*a, *Urtica dioica*) had also inhibitory effect of HMG-CoA reductase. Among them, the extract of *R. damascena* was found to be the most potent one [99].

The discovery of new effective and safe in long-term application therapeutics is essential for the control and prevention of obesity-related diseases. In this respect, the potential of medicinal and edible plants is still to be explored.

5. Conclusions

The summarized scientific data give a concept about the mechanisms behind the healing effects of plants traditionally used in Bulgarian folk medicine and traditional diet. The selected plants and their active compounds could exert their hypoglycemic and antiobese effects by affecting simultaneously several molecular markers in various processes from carbohydrate and lipid metabolism. Moreover, along with their insulin-like properties, many of the plants can stimulate the insulin secretion. This makes them invaluable in prevention and therapy of socially significant diseases such as diabetes and cardiovascular diseases. Despite the capacity of biotechnology methods to develop new therapeutics, it may be worth to turn a look at the natural resources which potential is still unrevealed.

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