https://doi.org/10.31925/farmacia.2022.6.4 **REVIEW**

SHORT REVIEW ON BIOACTIVE COMPOUNDS RECOVERED FROM VEGETAL WASTE AS A NEW TOOL IN DIABETES, OBESITY AND DYSLIPIDAEMIA PREVENTION AND TREATMENT

SIMONA SPÎNU, ALINA ORȚAN *, CATALINA VOAIDEȘ

University of Agronomic Sciences and Veterinary Medicine of Bucharest, 59 Mărăști Boulevard., 011464 Bucharest, Romania

**corresponding author: alina.ortan@fifim.ro*

Manuscript received: June 2022

Abstract

Following the processing of vegetal material, impressive amounts of vegetal waste are produced at global level. Currently, vegetal waste management from industries that use vegetal material are of interest at international level, both for economic and environmental reasons. Metabolic diseases are clinical manifestations characterized by comorbidities as obesity, arterial hypertension, dyslipidaemia and diabetes, which induce low-grade inflammation and oxidative stress. In recent years, for the prevention and treatment of metabolic diseases, the development of new therapeutic strategies, with fewer side effects, based on bioactive compounds resulting mainly from plant waste, has been attempted. These biocompounds have various beneficial effects on lipid and glucose metabolism, blood pressure, oxidative stress and body weight. The aim of this short review is to highlight the bioactive compounds recovered from vegetal waste as a new tool in diabetes, obesity and dyslipidaemia prevention and treatment.

Rezumat

În urma prelucrării materialului vegetal, la nivel global se produc cantități impresionante de deșeuri vegetale. În prezent, gestionarea deșeurilor vegetale din industriile care utilizează material vegetal prezintă interes la nivel internațional, atât din motive economice, cât și de mediu. Bolile metabolice sunt manifestări clinice caracterizate prin comorbidități precum obezitatea, hipertensiunea arterială, dislipidemia și diabetul, care induc inflamație de grad scăzut și stres oxidativ. In ultimii ani, pentru prevenția și tratamentul bolilor metabolice s-a încercat dezvoltarea de noi strategii terapeutice, cu mai puține efecte secundare, bazate pe compuși bioactivi rezultați în principal din deșeuri vegetale. Aceștia au diverse efecte benefice asupra metabolismului lipidelor și glucozei, tensiunii arteriale, stresului oxidativ și greutății corporale. Scopul acestei scurte recenzii este de a evidenția compușii bioactivi recuperați din deșeurile vegetale ca un nou instrument în prevenirea și tratamentul diabetului, obezității și dislipidemiei.

Keywords: plant waste, bioactive compounds, dyslipidemia, obesity, diabetes

Introduction

Metabolic diseases are the pathologies associated with disruption of normal metabolism, that involve impairment of the conversion of macronutrients from food (proteins, fats and carbohydrates) into energy, through a set of chemical reactions at the cellular level. Metabolic diseases that affect an increasing number of people (both adults and children) are diabetes, dyslipidaemia and obesity. The latest statistics show that 61 million adults in Europe and 537 million adults at global level [78] are affected by diabetes, 1.7 billion adults at global level are estimated to be affected by dyslipidaemia by 2027 [79] and 215 million adults with BMI (body mass index) ≥ 30 kg/m^2 in Europe are estimated to suffer from obesity by 2030 and 892 million adults globally by 2025 [77]. These numbers are worrying, especially in the context of the fact that there is a large number of undiagnosed people who are living with one of these diseases. Furthermore, in 2021, 6.7 million deaths caused by diabetes were registered (one every 5 seconds) [78]. The conventional treatments used for decades to prevent or treat metabolic diseases are not always suitable for patient particularities, inducing side effects, even severe complications that can lead to death. Conventional treatment in the case of diabetes consists in regulating blood sugar through subcutaneous insulin injections or drug administration (metformin, sulfonyl-urea, canagliflozin, dapagliflozin and empagliflozin). In addition to the recommendations related to changing the lifestyle by avoiding food products containing starch and introducing vegetable products rich in micronutrients, dietary fibres and polyphenols-rich sources into the diet, daily physical activity, etc., numerous drugs have been put on the market over time to reduce obesity. These, with or without an effect on weight loss, had numerous side effects (depression, anorexia, onset of cardiovascular diseases, etc.), with a direct threat to human health. Therefore, many have been withdrawn, and at the moment there is no effective therapeutic strategy regarding obesity. Dyslipidaemia is conventionally treated with statins, fibrates or niacin. Side effects such as diarrhoea, abdominal pain, metallic taste, lactic acidosis, mycotic genital infections, urinary infections, leg pain or diabetic ketoacidosis have been observed through the administration of conventional treatments. Thus, in all metabolic diseases, physical activities and a healthy diet are recommended, but, since these are not sufficient in most cases, the aim is to find new, effective, low-cost alternative treatments that eliminate unwanted side effects. In this direction, herbal medicine and vegetal based treatments provide an alternative treatment method for metabolic diseases [12, 16, 45, 51, 75].

It is well known that plant waste is a biodegradable, easily accessible and sustainable bioresource. Therefore, in recent years, the focus has been on the valorisation of vegetal waste (waste from plants, fruits or vegetables) by extracting and purifying the remaining bioactive compounds, in order to develop new plant-based products that respond to the growing burden of metabolic diseases around the world.

Most of the industries that use plants as raw material (fruits, vegetables, seeds and aerial parts) for various purposes, produce a large amount of solid waste that is still rich in bioactive compounds as phenolic compounds, flavonoids, tannins, terpenes, phytosterols, bioactive peptides, flavanols, fatty acids, volatile oils or anthocyanins. The treatment of metabolic diseases such as diabetes, dyslipidaemia and obesity continues to be a topic of current interest in alternative medicine based on bioactive compounds recovered from plant waste. In addition, the current trend is for the use of green approaches in the valorisation of plant wastes, targeting their bioconversion into high-value bio-products.

This short-review aims to present the green techniques used in the valorisation of plant waste resulted resulting from the processing of aromatic and medicinal plants, fruits, vegetables, aerial parts of plants, trees and shrubs. The recovered bioactive compounds are presented as an important tool of therapeutic approaches with potential use in the treatment of metabolic diseases.

Materials and Methods

The article collection methodology included the survey of three scientific databases (ScienceDirect, ScienceDirect, Pubmed and Scopus) for published research data, which took place over the last six months, starting in May 2022. Only papers written in English were considered, dating as far back as 2018. The electronic search was performed using as specific keywords: vegetal waste valorisation, plant waste valorisation, fruits waste valorisation, metabolic diseases and plant waste valorisation, vegetal waste green extraction methods, lipid metabolism, glucose metabolism, bioactive compounds, oxidative stress, etc. Title and abstracts retrieved by these searches were screened for relevance and deduplication. The selected articles were classified by article type (original research or review) and the validation was performed manually (by reading the entire article).

Current strategies for vegetal waste valorisation

Vegetal waste - a rich source of bioactive compounds

Large quantities of plant waste can accumulate not only during the processing of the plant material, but also during the harvesting and post-harvest stages. Thus, any part of the plant that is not subject to processing can be considered vegetal waste. An alternative to reduce the amount of unexploited waste with a negative impact on the environment is represented by their valorisation through green extraction, isolation and purification of bioactive compounds in order to obtain added value products, useful in the prevention and treatment of various maladies.

Numerous studies have shown that vegetable waste is an important and low-cost source of primary and secondary metabolites with medicinal and nutritional value, such as phenolic compounds (phenolic acids [20, 38, 67, 76], flavonoids [14, 18, 20, 22, 23, 34, 42, 56, 65, 71, 74], anthocyanins [20, 21, 35, 57, 71], vitamins (vitamin A [25], vitamin E [21], vitamin D [25], vitamin C [21, 25, 65, 74], amino acids [25], alkaloids [11, 18], glucosinolates [23], fatty acids [21], poly-saccharides [55], terpenes [14, 38, 57, 74].

Extraction techniques of vegetal waste material

The extraction process is a critical step for obtaining the targeted bioactive compounds. Currently, many of the new extraction techniques fall into the field of "green chemistry". According to "green strategies" this critical step implies, at an affordable cost, the reduction of extraction time, energy consumption and the amount of solvents, with the important consequence of increasing the positive impact on the environment.

In this regard, as a sustainable alternative are non-conventional extraction methods such as Ultrasound Assisted Extraction (UAE) [71], Microwave Assisted Extraction (MAE) [56], Solvent-Free Microwave Extraction (SFME) [5, 15], Supercritical Fluid Extraction (SFE) [74], Accelerated Solvet Extraction (ASE) [61], matrix solid-phase dispersion (MSPD) extraction [42], Infrared Assisted Extraction (IAE) [72] that outperform the conventional extraction methods as maceration, stirring, solvent extraction or Soxhlet extraction. Moreover, recently extraction techniques have been developed that combine non-conventional extraction methods with deep eutectic solvents (DESs) [73].

The selection of an extraction method depends on certain important requirements such as the nature of the compounds of interest, the degree of purity of the extract, the costs and the field of further use.

Thus, non-conventional extraction methods require the optimization of several parameters such as extraction time, ratio of plant material to the solvent, type of solvent (water, ethanol, methanol, etc.), degree of shredding of the plant material, working temperature, etc.

Isolation and purification techniques of bioactive compounds

Despite the progress made in the last decades, the steps of isolation, purification, identification, and characterization of the bioactive compounds recovered from plant waste extracts still require improvements and adjustments, especially from the point of view of increasing therapeutic efficacy. Significant progress has been registered in terms of chromatographic techniques for the separation and purification of bio-active compounds of different polarities. The traditional chromatographic technique such as Thin Layer Chromatography (TLC) is increasingly being replaced by modern chromatographic techniques such as Gas Chromatography (GC), High Performance Liquid Chromatography (HPLC), Ultra-High-Performance Liquid Chromatography-Electrospray Ionization Quadrupole Time-of-Flight Mass Spectrometry (UHPLC-ESI-QTOF/MS) [2], Centrifugal Partition Chromatography (CPC) [66] for various advantages as high purification of compounds (> 99%), faster compounds separation and isolation by different stationary phases.

Bioactive compounds isolated from vegetal waste used in prevention or treatment of metabolic diseases

Numerous studies indicate that plant waste is an important source of secondary metabolites. Secondary metabolites are known for their proven biological properties, such as antioxidant, anti-inflammatory, antibacterial, antiviral, anticancer and health-promoting effect against neurodegenerative and cardiovascular diseases, diabetes, obesity, dyslipidaemia, etc.

Furthermore, the long-term intake of secondary metabolites induces an overall positive effect on human health.

In the case of the metabolic diseases discussed in this review paper – diabetes, dyslipidaemia and obesity – numerous studies have pointed out natural approaches to delaying their onset and progression.

Diabetes

Diabetes is diagnosed based on high levels of blood glucose. According to the World Health Organization (WHO), changes in glucose metabolism indicate diabetes, more precisely when patients have blood sugar > 110 mg/dL or show insulin resistance [54]. There are two forms of diabetes, type I and type II, which occur in both adults and children. In the case of type I diabetes, the pancreas does not secrete insulin or secretes it in insufficient quantities to function properly, pancreatic islet β cells are destroyed necessitating lifelong insulin treatment. In type II diabetes, the body is resistant to the effect of insulin or the pancreas does not produce enough insulin to maintain an adequate level of glucose in the blood.

This metabolic disease is a major cause of blindness, kidney failure, lower limb amputation heart attacks and stroke. Studies have shown that the incidence of diabetes is much higher in elderly people compared to middle-aged people [1].

Recent research in this field aims to study the anti-diabetic effects of secondary metabolites recovered from plant wastes, anti-glycaemic activity being targeted. These studies were mainly carried out by testing the inhibition effects on α-amylase and α-glucosidase, but also on lipid peroxidation, aldose-reductase, pancreatic lipase and 5-lipoxygenase (5-LOX).

The data found in the *in vivo* and *in vitro* studies identified in the specialized literature regarding the effect of secondary metabolites recovered from plant waste on blood sugar variations – an important parameter in the diagnosis of diabetes – are presented in Table I.

Table I

Bioactive compounds isolated from vegetal waste with therapeutic application in diabetes

Vegetal waste origin	Bioactive compound	Studies
Musa paradisiaca (Var. Nanjangud rasa bale) - pseudostem	Stigmasterol, β-Sitosterol	[59]
Musa acuminate - male flowers and bracts	Lupeol, Umbelliferone	[14]
Musa (ABB – Nam Wa Mali-Ong) - inflorescences	Phytosphingosine, Xestoaminol-C, Adenine, 2-Amino-3-methyl-1-Butanol, α-Linolenic Acid, Stearic acid	[2]
Punica granatum - leaves	Gallic acid, Ellagic acid, Apigenin	[58]
Punica granatum - peel	Ellagic acid, B carboxylic acid, tannic acid, gallic acid, punicalagin, punicalin	[26, 31, 36, 43]
Allium cepa L. - waste	Quercetin-3,4′-O-diglucoside, Quercetin-4′-O-monoglucoside, Quercetin	[53]
Citrus sinensis L.- stem bark	Not specified	[6]
Persea americana - seeds	Not specified	[6]
Cynara Scolymus L. – floral stems	1-O-Caffeoylquinic acid, Luteolin-7-O-neohesperidoside, 1,5-Di-caffeoylquinic acid, Luteolin, Apigenin, Luteolin-7-O-glucoside (cynaroside)	[47]

Vegetal waste origin	Bioactive compound	Studies
Momordica cymbalaria - skin and seed	Not specified	[24]
Codonopsis pilosula - residue	Arabinose, glucose, galactose	[41]
Artocarpus odoratissimus – peel, seed	Phenolics, flavonoids	[33]
Mangifera odorata L. – peel, seed, kernel	β-Carotene, Ascorbic acid, α-Tocopherol, (±)-Naringenin, 2-Hydroxy-3,4-dimethoxybenzoic acid, apigenin 7-(2''-E-p-coumaroylglucoside), isovitexin	[37]
Mangifera indica L. - seed	Not specified	[7]
Crocus sativus - petals	Delphinidin 3,7-O-diglucoside, Petunidin 3,7-O-diglucoside, Malvidin O-glucoside, Kaempferol-3-O-sophoroside, Kaempferol-3-O-glucoside, Quercetin-3-7-O-diglucoside	[50]
Chukrasia tabularis A. Juss. - leaves	Kaempferol, Quercetin, Luteolin, Isorhamnetin, epiafzelechin-(4β-8)-catechin, 3,7,4′-trihydroxyflavan	[4]
Prunus tomentosa – seed	Aromatic glycosides	[40]

In an investigation carried out by [59] regarding the antiglycaemic activity have been tested *in vitro* the inhibitory activity of the isolated compounds against Type VI-B porcine pancreatic *α-amylase* (by 3,5-di-nitrosalicylic acid (DNS) assay) and yeast type-1 *α-glucosidase* (by the substrate *p*-nitrophenyl-α-D-gluco-pyranoside (*p*NPG)) enzymes, using acarbose as positive control. The *α-amylase* inhibitory effect of Stigmasterol (IC_{50}: 42.58 ± 2.14 µg/mL) and β-Sitosterol (IC_{50}: 43.43 ± 1.03 µg/mL) were significantly lower than positive control ($IC5_0$: 29.71 ± 1.51 µg/mL), comparatively with the *α-glucosidase* inhibitory effect where Stigmasterol (IC_{50}: 7.31 ± 0.12 µg/mL) and β-Sitosterol (IC_{50}: 7.80 ± 0.93 µg/mL) were significantly higher than positive control ($IC5_0$: 9.68 ± 0.48 µg/mL) thereby proving that the isolated bioactive compounds exhibit antiglycaemic activity.

The lupeol and umbelliferone isolated compounds from banana flower ethanolic extracts (95%), showed *α-amylase* (31.75%) (tested by DNS assay), *α-glucosidase* (84.17%) (tested using *p*NPG substrat) and lipase (70.59%) (tested using p-nitrophenylpalmitate substrat) inhibition by *in vitro* tests [14].

Diabetic rats treated for 45 days with methanolic extract of *Punica granatum* leaves (400 mg/kg) exhibited a significant decrease of blood glucose levels (107 ± 3.8 mg/dL), an increase in plasma insulin levels (14.7 ± 1.16 mg/dL), lower TC (150 ± 5.30 mg/dL) and lower TG (86.3 ± 3.90 mg/dL) [58].

The fractionated extracts from yellow onion waste [53] showed a remarkable inhibition of α-amylase activity (pancreatic porcine enzyme) (IC_{50} 48.2 ± 1.3 - 60.8 ± 1.6 µg/mL) and α-glucosidase (intestinal rat enzyme) (IC_{50} 42.5 ± 1.9 - 65.5 ± 1.5 µg/mL) compared to Acarbose positive control. The bioactive compounds extracted from onion waste (quercetin-3,4′-O-diglucoside, quercetin-4′-O-monoglucoside and quercetin) also showed significant inhibitory activity of α-amylase (IC_{50} 60.7 ± 1.3 - 75.5 ± 1.8 µg/mL) and α-glucosidase (IC_{50} 55.3 ± 1.2 - 70.5 ± 2.1 µg/mL). More, fractionated extracts from onion waste diluted in methanol, ethanol and ethyl acetate showed higher activities of inhibition of α-amylase and α-glucosidase compared to isolated flavonol extracts.

Prunus tomentosa seed waste extracts (70% ethanol), were successively fractionated with petroleum ether, ethyl acetate and n-butanol [40] isolating 11 aromatic glycosides. Two of the identified glucosides presented inhibitory activity on α-glucosidase (IC_{50}: - 4.27 mg/mL, respectively 4.34 mg/mL) similar to that of the positive control Acarbose (IC_{50}: - 4.16 mg/mL), and it could be developed as a safe and effective anti-diabetic basic element.

Dyslipidaemia

Dyslipidaemia is an asymptomatic disease that occurs when there are quantitative changes in blood concentrations of one or more of the following parameters: total cholesterol (TC), triglycerides (TG), low-density lipo-protein cholesterol (LDL-C) or high-density lipoprotein big cholesterol (HDL-C). According to the International Diabetes Foundation alterations in lipid metabolism indicates dyslipidaemia, more specifically it occurs when the patients have HDL-C < 40 mg/dL (men) or HDL-C < 50 mg/dL (women) or TG > 150 mg/dL [54].

Genetic predisposition and external factors part of lifestyle (high consumption of saturated fats, fried foods or alcohol; smoking; sedentarism or long-term administration of certain medicines) are considered causes of dyslipidaemia. Dyslipidaemia classification includes *primary dyslipidaemia* or hyperlipidaemia divided in hypertriglyceridaemia, hypercholesterolaemia, high-density lipoprotein decreases; *combined dyslipidaemia* and *secondary dyslipidaemia* [49]. Being a lipid metabolism disorder, it is standard diagnosticated by a lipid profile.

At the same time, dyslipidaemia is one of the risk factors that significantly contribute to cardiovascular diseases, especially atherosclerosis [49]. Dyslipidaemia is associated with diabetes, both type I and type II [64, 68], through low HDL-C, high TG and LDL-C levels.

Researches regarding anti-dyslipidaemic effects of secondary metabolites present in plant waste extracts were performed by testing lipid accumulation inhibition and levels of plasma TC, TG and HDL-c, because those parameters are followed in this metabolic disease.

Few results regarding the effect of secondary metabolites isolated from vegetal waste on lipid metabolism (*in vivo* or *in vitro* studies) were identified in the studied articles. From the data found in the specialized literature, Table II presents studies on the modulation of lipid metabolism, the decrease of plasma TC and TG, respectively the increase of plasma HDL-c.

Table II

Bioactive compounds isolated from vegetal waste with therapeutic application in dyslipidemia

Vegetal waste origin	Bioactive compound	Studies
Citrus sinensis L. Osbeck - peel	Hesperidin	[69]
Prunus persica L. - peel	Epicatechin 3-O-gallate, Procyanidin dimer B2, Epicatechin 3-O-glucoside, gallocatechin 3-O-gallate, catechin, 5-caffeoylquinic acid, 3-caffeoylquinic acid, 5-feruloylquinic acid	[34]
Persea americana - seeds	Not specified	[10]
Beta vulgaris L. - leaves and stalk	Vitexin-2-O-Rhamnoside	[29]
Passiflora edulis - peel	Caffeic acid, isoorientin	[30]
Dendrobium officinale - leaves	Glucose, Mannose, Glucuronic acid, Galactose, Arabinose	[27]
Vitis vinifera 'Merlot' - grape pomace	Gallic acid, Catechin, Epicatechin, p-Coumaric acid, Ellagic acid, Quercetin, Chlorogenic acid, Resveratrol	[17]

Citrus waste valorisation (citrus peels) in order to obtain certain chemical compounds of great interest has gained momentum recently. Thus, hesperidin was purified from plant wastes such as orange or tangerine peels. This is a flavone glycoside and an essential raw material for synthesizing diosmetin (5,7,3'-trihydroxy-4'-methoxyflavone) [48, 63, 69]. In a study conducted by Meephat *et al*. [46], the dyslipidaemic effect of diosmetin was highlighted in rats with metabolic syndrome induced with high-fat diet plus 15% fructose in drinking water.

Methanolic extracts from peach waste (peel), containing a total polyphenol content of 80.68 ± 1.12 mg GAE/g dried mass, significantly remitted lipid accumulation in mice fed with a high-fat diet, decreased serum and liver lipid levels and increased excretion of TG, TC and total bile acids in feces (studies have been carried out by commercial kits) [34], due to high contents of flavanols and hydroxycinnamic acids. Moreover, an improvement in the symptoms of fatty liver, as well as dark liver tissue was observed.

Obesity

Obesity is defined as excessive fat accumulation with a risk to health, that occurs when a body mass index (BMI) is over 30 kg/m^2, associated with co-morbid metabolic and chronic diseases, including low-grade inflammation, metabolic syndrome, type 2 diabetes, elevated blood glucose, insulin resistance, cardiovascular diseases, etc. [52]. Systemic oxidative stress, reduced antioxidant defences and adipokine imbalance are associated with obesity, as well as dyslipidaemia, through elevated TG, very LDL, normal or slightly elevated LDL-C and non-HDL-C levels. Dysregulation of lipid metabolism (synthesis, decomposition, digestion, absorption processes and transport of lipids) [32] is considered the main cause of obesity.

Table III

Bioactive compounds isolated from vegetal waste with therapeutic application in obesity

Vegetal waste origin	Bioactive compound	Studies
Prunus persica L. - peel and remnant pulp after juice extraction	4-caffeoylquinic acid, 3-caffeoylquinic acid, p-coumaroylquinic acid, 4-feruloylquinic acid, Quercetin 3-O-rutinoside, Kaempferol 3-O-rutinoside, Quercetin 3-O-rhamnosyl-galactoside, Ellagic acid glucoside, Gallic acid 4-O-glucoside	[62]
Myrciaria Jaboticaba (Vell.) Berg - peel	Cyanidin-3-O-glucoside, Ellagic acid	[39]
Malpighia emarginata - peel, residual pulp, seeds	Quercetin, Quercetin-3-glycoside, Rutin, 1-kestose, Malic acid, Succinic acid, Formic acid, Ascorbic acid.	[9]
Lippia graveolens - stem	Naringenin, Taxifolin, Eriodictyol, Caffeic acid, Cummaric acid, Quercetin 3-O-glycoside, 2-Hydroxybenzoic acid, Apigeninm Luteolin	[28]
Vaccinium spp. - Blueberry pomace	Not specified	[13]
Musa acuminata x *balbisiana* BBB - peel	Pectin	[8]
Punica granatum - peel	Ellagic acid, B carboxylic acid, Tannic acid, Gallic acid, (−) epigallocatechin gallate, 3′,4′,5, 7-tetrahydroxyisoflavanone, 6″-O-acetyldaidzin, cyanidin 3-O-xyloside, dihydroquercetin 3-O-hexoside	[44, 60]
Passiflora edulis - peel	Flavonoids, carotenoids, β-carotene, Ferulic acid	[70]
Hibiscus sabdariffa L. - exhausted calyces	Caffeoylquinic acid isomer I, Coumaroylquinic acid isomer I, Gallic acid, Ellagic acid, Feruoylquinic acid isomer II, Dicaffeoylquinic acid	[3]
Euterpe oleracea Mart. - seed	Phenolic compounds	[19]

An alternative for the treatment of obesity is represented by lowering the serum level of glucose, TG and insulin, by administering extracts or products enriched with secondary metabolites recovered from plant wastes.

Weight loss is the targeted result. Table III shows selected data from the specialized literature where plant waste has proven to be a rich source of bioactive compounds with anti-obesity effects.

Peach juice by-products (skins and pulp resulting from juice extraction), proved to be a rich source of polyphenols, and their extracts administered as supplements to obese rats led to lower serum glucose levels, lower TG (identified using commercial enzyme-colorimetric kits) and lower serum insulin levels. (quantified using an ELISA kit) [62].

Also, in a study conducted on diet-induced obese rats for 12 weeks [39], the effects of freeze-dried jaboticaba peel powder and aqueous jaboticaba peel extract were investigated. Results showed reduced weight gain, adiposity and improved insulin sensitivity, as well as increased HDL-cholesterol levels and prevented hepatic steatosis, proving to be an adequate strategy to prevent or control obesity.

Acerola (*Malpighia emarginata*) (peel, residual pulp, seeds) waste extracts, orogastric administrated by gavage, reduced the weight of rats fed with a high-fat diet, decreased the serum TG, TC, LDL levels and increased HDL level [9]. Also, administration of acerola extracts increased the cellular glucose uptake and showed a good tolerance to insulin action on glucose level.

Conclusions

Herbal therapy is based on empirical findings of hundreds of years and continues to provide mankind with new remedies, plants, fruits and vegetables being available, low-cost and safe resources with high potential for the treatment or prophylaxis of a disease. The pharmaceutical industry worldwide has identified this opportunity, continuing to investigate promising leads from natural products in their effort to develop new drugs that meet modern FDA standards of quality, safety and efficacy.

Moreover, recent studies have shown that plant waste resulting from the processing of plant material is a rich and renewable source of bioactive compounds. The development of the appropriate method for obtaining bioactive compounds depends mainly on their solubility and stability, but also on the costs related to the scale-up of the process at industrial level. Bioactive compounds recovered from plant waste, as presented in this review, are promising tools for maintaining human health. Most of the vegetal waste identified in the selected studies results from the processing of fruits and vegetables, which indicates an increased interest in this direction, considering the daily consumption of fruits and vegetables globally. According to the literature study carried out regarding the different types of vegetable waste and their utilization, it can be observed that there are numerous studies that confirm the anti-dyslipidaemic, anti-diabetic and anti-obesity activity of the purified bioactive compounds.

Acknowledgement

The authors gratefully acknowledge the support obtained through a grant of the Romanian Ministry of Education and Research, CCCDI-UEFISCDI, project No. PN-III-P3-3.5-EUK- 2019-0226, within PNCDI III.

Conflict of interest

The authors declare no conflict of interest.

References

1. Abdelhafiz AH, Sinclair AJ, Diabetes in the elderly. *Medicine*, 2022; 50(11): 737-740.
2. Aiemcharoen P, Wichienchot S, Sermwittayawong D, Antioxidant and anti-diabetic activities of crude ethanolic extract from the banana inflorescence of *musa* (ABB group) namwa maliong. *Funct Foods Health Dis.*, 2022; 12(4): 161-174.
3. Amaya-Cruz D, Peréz-Ramírez IF, Pérez-Jiménez J, Nava GM, Reynoso-Camacho R, Comparison of the bioactive potential of Roselle (*Hibiscus sabdariffa* L.) calyx and its by-product: Phenolic characterization by UPLC-QTOF MSE and their anti-obesity effect *in vivo*. *Food Res Int.*, 2019; 126: 108589: 1-9.
4. Andrade C, Ferreres F, Gomes NGM, Gil-Izquierdo A, Duangsrisai S, Pereira DM, Andrade PB, Saklayen PV, Valorisation of the industrial waste of *Chukrasia tabularis* A. Juss.: Characterization of the leaves phenolic constituents and antidiabetic-like effects. *Ind Crops Prod.*, 2022; 185: 115100.
5. Araujo ARTS, Périno S, Fernandez X, Cunha C, Rodrigues M, Ribeiro MP, Jordao L, Silva LA, Rodilla J, Coutinho P, Chemat F, Solvent-Free Microwave Extraction of *Thymus mastichina* essential oil: influence on their chemical composition and on the antioxidant and antimicrobial activities. *Pharmaceuticals*, 2021; 14(8): 709: 1-13.
6. Azantsa BGK, Takuissu GR, Tcheumeni EJ, Fonkoua M, Dibacto ERK, Ngondi JL, Oben JE, Antihyperglycemic mechanisms of *Allium sativum*, *Citrus sinensis* and *Persea americana* Extracts: Effects on inhibition of digestive enzymes, glucose adsorption and absorption on yeast cells and psoas muscles. *Diabetes Res Open J.*, 2019; 6(1): 1-9.
7. Azhar A, Aamir K, Asad F, Kazi HA, Farooqui MU, Therapeutic effect of mango seed extract in diabetes mellitus. *Professional Med J.*, 2019; 26(09): 1551-1556.
8. Bagabaldo PAA, Atienza LM, Castillo-Israel KAT, Estacio MAC, Gaban PJV, Maniwang JRC, Gapasin RP, Estribillo AGM, Cena-Navarro RB, 'Saba' banana (*Musa acuminata* x *balbisiana* BBB Group) peel pectin supplementation improves biomarkers of obesity and associated blood lipid disorders in obese hyper-cholesterolemic mice. *Curr Res Food Sci.*, 2022; 5: 251-260.
9. Batista KS, Soares NL, Dorand VAM, Alves AF, Lima MS, Pereira RA, Souza EL, Magnani M, Persuhn DC, Aquino JS, Acerola fruit by-product

alleviates lipid, glucose, and inflammatory changes in the enterohepatic axis of rats fed a high-fat diet. *Food Chem.*, 2023; 403: 134322.
10. Boris KGA, Ntentie FR, Mbong AM, Mafongang A, Kamtchoum A, Momo C, Chimou NL, Fonkoua M, Edoun EF, Ngondi JL, Julius EO, Lipomodulatory and anti-oxidative stress effects of a polyherbal formulation based on garlic and avocado seed extracts on high fat high sucrose diet fed rats. *Metab Open*, 2022; 15: 100195: 1-8.
11. Calcio Gaudino E, Colletti A, Grillo G, Tabasso S, Cravotto G, Emerging processing technologies for the recovery of valuable bioactive compounds from potato peels. *Foods*, 2020; 9: 1598: 1-19.
12. Chaachouay N, Benkhnigue O, Fadli M, El Ibaoui H, Zidane L, Ethnobotanical and ethnopharmacological studies of medicinal and aromatic plants used in the treatment of metabolic diseases in the Moroccan Rif. *Heliyon*, 2019; 5(10): e02191: 1-9.
13. Chai Z, Yan Y, Zan S, Meng X, Zhang F, Probiotic-fermented blueberry pomace alleviates obesity and hyperlipidemia in high-fat diet C57BL/6J mice. *Food Res Int.*, 2022; 157: 111396.
14. Chiang SH, Yang KM, Lai YC, Chen CW, Evaluation of the *in vitro* biological activities of Banana flower and bract extracts and their bioactive compounds. *Int J Food Prop.*, 2021; 24: 1-16.
15. Chouhan KBS, Tandey R, Sen KK, Mehta R, Mandal V, A unique model of gravity assisted solvent free microwave based extraction of essential oil from mentha leaves ensuring biorefinery of leftover waste biomass for extraction of nutraceuticals: towards cleaner and greener technology. *J Clean Prod.*, 2019; 225: 587-598.
16. Chu S, Zhang F, Wang H, Xie L, Chen Z, Zeng W, Zhou Z, Hu F, Aqueous extract of guava (*Psidium guajava* L.) leaf ameliorates hyperglycemia by promoting hepatic glycogen synthesis and modulating gut microbiota. *Front Pharmacol.*, 2022; 13: 907702: 1-13.
17. Daniel T, Ben-Shachar M, Drori E, Hamad S, Permyakova A, Ben-Cnaan E, Tam J, Kerem Z, Rosenzweig T, Grape pomace reduces the severity of non-alcoholic hepatic steatosis and the development of steatohepatitis by improving insulin sensitivity and reducing ectopic fat deposition in mice. *J Nutr Biochem.*, 2021; 98: 108867.
18. da Silva GG, Pimenta LPS, Melo JOF, Mendonça HOP, Augusti R, Takahashi JA, Phytochemicals of avocado residues as potential acetylcholinesterase inhibitors, antioxidants, and neuroprotective agents. *Molecules*, 2022; 27(6): 1892: 1-18.
19. da Silva RC, Batista A, Costa DCFD, Moura-Nunes N, Koury JC, da Costa CA, Resende ÂC, Daleprane JB, Açai (*Euterpe oleracea* Mart.) seed flour prevents obesity-induced hepatic steatosis regulating lipid metabolism by increasing cholesterol excretion in high-fat diet-fed mice. *Food Res Int.*, 2018; 111: 408-415.
20. de Andrade RB, Machado BAS, Barreto GA, Correa LC, Leal IL, Tavares P, Ferreira ES, Umsza-Guez MA, Syrah grape skin residues has potential as source of antioxidant and anti-microbial bioactive compounds. *Biology*, 2021; 10: 1262: 1-15.
21. Dias M, Caleja C, Pereira C, Calhelha RC, Kostic M, Sokovic M, Tavares D, Baraldi IJ, Barros L, Ferreira I, Chemical composition and bioactive properties of byproducts from two different kiwi varieties. *Food Res Int.*, 2020; 127: 108753.
22. Dominguez-Rodriguez G, Garcia MC, Plaza M, Marina ML, Revalorization of Passiflora species peels as a sustainable source of antioxidant phenolic compounds. *Sci Total Environ.*, 2019; 696: 134030: 1-13.
23. Drabinska N, Jez M, Nogueira M, Variation in the accumulation of phytochemicals and their bioactive properties among the aerial parts of Cauliflower. *Antioxidants*, 2021; 10: 1597: 1-13.
24. Elangovan A, Subramanian A, Durairaj S, Ramachandran J, Lakshmanan DK, Ravichandran G, Lakshmanan DK, Ravichandran G, Nambirajan G, Thilagar S, Antidiabetic and hypolipidemic efficacy of skin and seed extracts of *Momordica cymbalaria* on alloxan induced diabetic model in rats. *J Ethnopharmacol.*, 2019; 241: 111989: 1-11.
25. Enemor VHA, Oguazu CE, Odiakosa AU, Okafor SC, Evaluation of the medicinal properties and possible nutrient composition of *Citrullus lanatus* (Watermelon) Seeds. *Res J Med Plants*, 2019; 13: 129-135.
26. Faddladdeen KAJ, Ameliorating effect of pomegranate peel extract supplement against type 1 diabetes-induced hepatic changes in the rat: biochemical, morphological and ultrastructural microscopic studies. *Folia Morphol (Warsz)*, 2021; 80(1): 149-157.
27. Fang J, Lin Y, Xie H, Farag MA, Feng S, Li J, Shao P, *Dendrobium officinale* leaf polysaccharides ameliorated hyperglycemia and promoted gut bacterial associated SCFAs to alleviate type 2 diabetes in adult mice. *Food Chem X*, 2022; 13: 100207: 1-12.
28. Frías-Zepeda ME, Rosales-Castro M, Escalona-Cardoso GN, Paniagua-Castro N, Ethanolic extract of *Lippia graveolens* stem reduce biochemical markers in a murine model with metabolic syndrome. *Saudi J Biol Sci.*, 2022; 29(12): 103422: 1-7.
29. Gomes APO, Ferreira MA, Camargo JM, Araújo MO, Mortoza AS, Mota JF, Coelho ASG, Capitani CD, Coltro WKT, Botelho PB, Organic beet leaves and stalk juice attenuates HDL-C reduction induced by high-fat meal in dyslipidemic patients: A pilot randomized controlled trial. *Nutrition*, 2019; 65: 68-73.
30. Goss MJ, Nunes MLO, Machado ID, Merlin L, Macedo NB, Silva AMO, Bresolin TMB, Santin JR, Peel flour of *Passiflora edulis* Var. Flavicarpa supplementation prevents the insulin resistance and hepatic steatosis induced by low-fructose-diet in young rats. *Biomed Pharmacother.*, 2018; 102: 848-854.
31. Grabež M, Škrbić R, Stojiljković MP, Rudić-Grujić V, Paunović M, Arsić A, Petrović S, Vučić V, Mirjanić-Azarić B, Šavikin K, Menković N, Janković T, Vasiljevićg N, Beneficial effects of pomegranate peel extract on plasma lipid profile, fatty acids levels and blood pressure in patients with diabetes mellitus type-2: a randomized, double-blind, placebo-controlled study. *J Funct Foods*, 2020; 64: 103692: 1-8.
32. Hou C, Zhang W, Li J, Du L, Lv O, Zhao S, Li J, Beneficial Effects of Pomegranate on Lipid Metabolism in Metabolic Disorders. *Mol Nutr Food Res.*, 2019; 63(16): e1800773: 1-12.

33. Jonatas KAS, Querequincia JMB, Miranda SD, Obatavwe U, Corpuz MJA, Vasquez RD, Antidiabetic evaluation of *Artocarpus odoratissimus* (Moraceae) fruit. *J Ilmiah Farm.*, (2020); 16(1): 1-8.
34. Kan JA, Chen CC, Huo TB, Xie WJ, Hui YY, Liu J, Jin CH, Polyphenolic-enriched peach peels extract regulates lipid metabolism and improves the gut microbiota composition in high fat diet-fed mice. *J Funct Foods.*, 2020; 72: 104082: 1-12.
35. Kobo GK, Kaseke T, Fawole OA, Micro-encapsulation of phytochemicals in passion fruit peel waste generated on an organic farm: effect of carriers on the quality of encapsulated powders and potential for value-addition. *Antioxidants*, 2022; 11: 1579: 1-20.
36. Kumar YR, Narayanaswamy HD, Rao S, Satyanarayana ML, Nadoor P, Rathnamma D, Effects of pomegranate (*Punica granatum*) juice and peel extract on biochemical parameters in streptozotocin induced diabetic rats. *J Pharm Innov.*, 2022; 11(1S): 970-977.
37. Lasano NF, Hamid AH, Karim R, Dek MSP, Shukri R, Shazini Ramli N, Nutritional composition, anti-diabetic properties and identification of active compounds using UHPLC-ESI-Orbitrap-MS/MS in *Mangifera odorata* L. peel and seed kernel. *Molecules*, 2019; 24(2): 320: 1-20.
38. Lebaka VR, Wee YJ, Ye W, Korivi M, Nutritional Composition and Bioactive Compounds in Three Different Parts of Mango Fruit. *Int J Environ Res Public Health*, 2021;18: 741: 1-20.
39. Lenquiste SA, de Almeida Lamas C, da Silva Marineli R, Moraes ÉA, Borck PC, Camargo RL, Quitete VHAC, Carneiro EM, Junior MRM, Jaboticaba peel powder and jaboticaba peel aqueous extract reduces obesity, insulin resistance and hepatic fat accumulation in rats. *Food Res Int.*, 2019; 120: 880-887.
40. Liu QB, Cheng ZY, Yan ZY, Wang D, Bai M, Huang XX, Song SJ, *Prunus tomentosa* seed waste as a source of aromatic glycosides: Valuable phytochemicals with α - glucosidase inhibitory and hepatoprotective properties. *Ind Crops Prod.*, 2018; 111: 590-596.
41. Liu W, Lv X, Huang W, Yao W, Gao X, Characterization and hypoglycemic effect of a neutral polysaccharide extracted from the residue of *Codonopsis Pilosula*. *Carbohydr Polym.*, 2018; 197: 215-226.
42. Loncaric A, Matanovic K, Ferrer P, Kovac T, Sarkanj B, Skendrovic Babojelic M, Lores M, Peel of traditional apple varieties as a great source of bioactive compounds: Extraction by Micro-Matrix Solid-Phase Dispersion. *Foods*, 2020; 9(1): 80: 1-18.
43. Malik LA, Ad'hiah AH, Aziz GM, Phytochemical content and the potential of *Punica granatum* peel extracts as radical scavengers and dipeptidyl peptidase-4 inhibitors. *J Biotechnol Res Center*, 2019; 13(1): 5-11.
44. Manna K, Mishra S, Saha M, Mahapatra S, Saha C, Yenge G, Gaikwad N, Pal R, Oulkar D, Banerjee K, Das Saha K, Amelioration of diabetic nephropathy using pomegranate peel extract-stabilized gold nano-particles: Assessment of NF-κB and Nrf2 signaling system. *Int J Nanomedicine*, 2019; 14: 1753-1777.
45. McGrath L, Fernandez ML, Plant-based diets and metabolic syndrome: Evaluating the influence of diet quality. *J Agric Food Res.*, 2022; 9: 100322: 1-9.
46. Meephat S, Prasatthong P, Rattanakanokchai S, Bunbupha S, Maneesai P, Pakdeechote P, Diosmetin attenuates metabolic syndrome and left ventricular alterations *via* the suppression of angiotensin II/AT1 receptor/gp91phox/p-NF-κB protein expression in high-fat diet fed rats. *Food Funct.*, 2021; 12(4): 1469-1481.
47. Mejri F, Baati T, Martins A, Selmi S, Luisa Serralheiro M, Falé PL, Rauter A, Casabianca H, Hosni K, Phytochemical analysis and *in vitro* and *in vivo* evaluation of biological activities of artichoke (*Cynara scolymus* L.) floral stems: Towards the valorization of food by-products. *Food Chem.*, 2020; 333: 127506: 1-10.
48. Montenegro-Landívar MF, Tapia-Quirós P, Vecino X, Reig M, Valderrama C, Granados M, Cortina JL, Saurina J, Fruit and vegetable processing wastes as natural sources of antioxidant-rich extracts: evaluation of advanced extraction technologies by surface response methodology. *J Environ Chem Eng.*, 2021; 9(4): 105330: 1-10.
49. Mosca S, Araújo G, Costa V, Correia J, Bandeira A, Martins E, Mansilha H, Tavares M, Coelho MP, Dyslipidemia diagnosis and treatment: risk stratification in children and adolescents. *J Nutr Metab.*, 2022; 4782344: 1-10.
50. Moshfegh F, Balanejad SZ, Shahrokhabady K, Attaranzadeh A, *Crocus sativus* (saffron) petals extract and its active ingredient, anthocyanin improves ovarian dysfunction, regulation of inflammatory genes and antioxidant factors in testosterone-induced PCOS mice. *J Ethnopharmacol.*, 2022; 282:114594: 1-12.
51. Mthiyane FT, Dludla PV, Ziqubu K, Mthembu SXH, Muvhulawa N, Hlengwa N, Nkambule BB, Mazibuko-Mbeje SE, A review on the antidiabetic properties of *Moringa oleifera* extracts: focusing on oxidative stress and inflammation as main therapeutic targets. *Front Pharmacol.*, 2022; 13:940572: 1-17.
52. Muller TD, Bluher M, Tschop MH, DiMarchi RD, Anti-obesity drug discovery: advances and challenges. *Nat Rev Drug Discov.*, 2022; 21: 201-223.
53. Nile A, Nile SH, Kim DH, Keum YS, Seok PG, Sharma K, Valorization of onion solid waste and their flavonols for assessment of cytotoxicity, enzyme inhibitory and antioxidant activities. *Food Chem Toxicol.*, 2018; 119: 281-289.
54. Noce A, Di Lauro M, Di Daniele F, Pietroboni Zaitseva A, Marrone G, Borboni P, Di Daniele N, Natural bioactive compounds useful in clinical management of metabolic syndrome. *Nutrients*, 2021; 13(2): 630: 1-33.
55. Petkowicz CLO, Williams PA, Pectins from food waste: Characterization and functional properties of a pectin extracted from broccoli stalk. *Food Hydrocoll.*, 2020; 107: 105930: 1-8.
56. Petrotos K, Giavasis I, Gerasopoulos K, Mitsagga C, Papaioannou C, Gkoutsidis P, Optimization of vacuum-microwave-assisted extraction of natural polyphenols and flavonoids from raw solid waste of the orange juice producing industry at industrial scale. *Molecules*, 2021; 26(1): 246: 1-27.

57. Pintac D, Majkic T, Torovic L, Orcic D, Beara I, Simin N, Mimica-Dukic N, Lesjak M, Solvent selection for efficient extraction of bioactive compounds from grape pomace. *Ind Crops Prod.*, 2018; 111: 379-390.
58. Pottathil S, Nain P, Morsy MA, Kaur J, Al-Dhubiab BE, Jaiswal S, Mechanisms of antidiabetic activity of methanolic extract of *Punica granatum* leaves in nicotinamide/streptozotocin-induced type 2 diabetes in rats. *Plants*, 2020; 9: 1609: 1-15.
59. Ramu R, Shirahatti PS, Deepika TH, Bajpe SN, Sreepathi N, Patil SM, Prasad MN, Investigating *Musa paradisiaca* (Var. Nanjangud rasa bale) pseudostem in preventing hyperglycemia along with improvement of diabetic complications. *J Appl Biol Biotechnol.*, 2022; 10(4): 56-65.
60. Ramzy M, Role of pomegranate peel on ameliorated hyperglycemia and hypercholesterolemia in experimental rats. *J Med Sci Clin Res.*, 2019; 2(3): 185-190.
61. Repajić M, Cegledi E, Kruk V, Pedisić S, Çınar F, Bursać Kovačević D, Žutić I, Dragović-Uzelac V, Accelerated Solvent Extraction as a Green Tool for the recovery of polyphenols and pigments from wild nettle leaves. *Processes*, 2020; 8(7): 803: 1-19.
62. Rodríguez-González S, Pérez-Ramírez IF, Amaya-Cruz DM, Gallegos-Corona MA, Ramos-Gomez M, Mora O, Reynoso-Camacho R, Polyphenol-rich peach (*Prunus persica* L.) by-product exerts a greater beneficial effect than dietary fiber-rich by-product on insulin resistance and hepatic steatosis in obese rats. *J Funct Foods*, 2018; 45: 58-66.
63. Šafranko S, Ćorković I, Jerković I, Jakovljević M, Aladić K, Šubarić D, Jokić S, Green extraction techniques for obtaining bioactive compounds from Mandarin peel (*Citrus unshiu* var. Kuno): phytochemical analysis and process optimization. *Foods*, 2021; 10(5): 1043: 1-16.
64. Shahwan MJ, Jairoun AA, Farajallah A, Shanabli S, Prevalence of dyslipidemia and factors affecting lipid profile in patients with type 2 diabetes. *Diabetes Metab Syndr: Clin Res Rev.*, 2019; 13(4): 2387-2392.
65. Sir Elkhatim KA, Elagib RAA, Hassan AB, Content of phenolic compounds and vitamin C and antioxidant activity in wasted parts of Sudanese citrus fruits. *Food Sci Nutr.*, 2018; 6: 1214-1219.
66. Spînu S, Orțan A, Ionescu D, Moraru I, Centrifugal partition chromatography (CPC) – a novel method of separation and purification of natural products – a short review. *Curr Trends Nat Sci.*, 2020; 9(18): 6-11.
67. Varga E, Fülöp I, Farczádi L, Croitoru MD, Polyphenolic determination from medicinal plants used in veterinary medicine by an UHPLC-LC-MS/MS method. *Farmacia*, 2020; 68(6): 1129-1135.
68. Vergès B, Dyslipidemia in Type 1 Diabetes: A masked danger. *Trends Endocrinol Metab.*, 2020; 31(6): 422-434.
69. Victor MM, David JM, Cortez MVM, Leite JL, da Silva GSB, A high-yield process for extraction of hesperidin from orange (*Citrus sinensis* L. osbeck) peels waste, and its transformation to diosmetin, A valuable and bioactive flavonoid. *Waste Biomass Valoriz.*, 2021; 12: 313-320.
70. Vuolo MM, Lima GC, Batista ÂG, Carazin CBB, Cintra DE, Prado MA, Júnior MRM, Passion fruit peel intake decreases inflammatory response and reverts lipid peroxidation and adiposity in diet-induced obese rats. *Nutr Res.*, 2020; 76: 106-117.
71. Wiliantari S, Iswandana R, Elya B, Total Polyphenols, Total Flavonoids, Antioxidant activity and inhibition of tyrosinase enzymes from extract and fraction of *Passiflora ligularis* juss. *Pharmacogn J.*, 2022; 14(3): 660-671.
72. Xiang B, Zhou X, Qin D, Li C, Xi J, Infrared assisted extraction of bioactive compounds from plant materials: Current research and future prospect. *Food Chem.*, 2022; 371: 131192.
73. Xu Z, Cai Y, Ma Q, Zhao Z, Yang D, Xu X, Optimization of extraction of bioactive compounds from *Baphicacanthus cusia* leaves by hydrophobic deep eutectic solvents. *Molecules*, 2021; 26(6): 1729: 1-13.
74. Yaqoob M, Aggarwal P, Babbar N, Extraction and screening of kinnow (*Citrus reticulata* L.) peel phytochemicals, grown in Punjab, India. *Biomass Convers Biorefin.*, 2022; https://doi.org/10.1007/s13399-021-02085-6.
75. Yu W, Zeng D, Xiong Y, Shan S, Yang X, Zhao H, Health benefits of functional plant polysaccharides in metabolic syndrome: An overview. *J Funct Foods*, 2022; 95: 105154: 1-12.
76. Zaman T, Irshad M, Khan MF, Mehmood A, Hussain I, Mahmood M, *In vitro* pharmacological evaluation of *Galium elegans*: phytochemical, antioxidant, biofilm inhibition and cytotoxicity potential. *Farmacia*, 2021; 69(6): 1159-1165.
77. https://data.worldobesity.org.
78. https://diabetesatlas.org.
79. www.globenewswire.com.