IDENTIFICATION AND CHARACTERIZATION OF ANTIDIABETIC AND ANTIHYPERTENSIVE AGENTS FROM THREE TRADITIONAL HERBAL MEDICINES

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THESIS ABSTRACT

Identification And Characterization of Antidiabetic And Antihypertensive Agents From Three Traditional Herbal Medicines

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Diabetes mellitus is a severe metabolic disorder due to either the inefficient use of the insulin or the pancreas dysfunction. From the data from World Health Organization (WHO), 422 million adults are suffering from diabetes, which means one in eleven people have diabetes. Typically, there are two types of diabetes mellitus: Type 1 diabetes (T1DM) and Type 2 diabetes (T2DM), and one especially type of diabetes mellitus: gestational diabetes mellitus (GDM), which is specific to the pregnancy period, and the condition usually disappears after pregnancy. Recently, type 2 diabetes mellitus (T2DM) has become a widespread, epidemic disease, especially in developing countries. Herbal remedies are traditional for T2DM treatment. In this research, three traditional remedies were chosen: *Khaya Senegalensis* (11L), *Anacardium Occidentale* (12M), and *Moringa Oleifera (*13N), which have traditionally been used as herbal remedies for T2DM management in some countries for an extended period. Unfortunately, the specific biologically active compounds for the T2DM treatment have not been identified and evaluated. The purpose of this research was to identify antidiabetic secondary metabolites of those three species.

Since T2DM is commonly accompanied by hypertension and obesity, Antihypertensive agents and anti-obesity agents were also checked. I hypothesize that only one or only small groups of

compounds (drugs) in those plants play a significant role in T2DM management. To test this hypothesis, extraction ion chromatogram (EIC) was used to identify the presence or absence of antidiabetic agents, antihypertensive agents, and anti-obesity agents based on the in-house Drug Library. Methanol+1% Acetic Acid was used to as the extraction method to extract compounds from crushed seeds, which have the great ability to reduce glucose levels in C57BL/6J mice from the previous work for this project. One hundred and eighty-five compounds were identified through HPLC/MS data analysis and acquisition from the previous analysis. The results showed that 11L contains three antidiabetic agents: NVP-DPP728, Voglibose, and Acetohexamide. Also, four antidiabetic agents were dissected and identified in 12M: A-769662, Acadesine, Voglibose, and Acetohexamide. There was any antidiabetic agent identified in 13N, but an Angiotensin II Receptor Blocker (ARB) was identified, which are a class of drugs used to manage hypertension, heart failure, and kidney failure, in 13N: ZD-6888. Also, 12M contains two β- blockers which are already approved drugs to control blood pressure by FDA: Carteolol and Nipradilol. Unfortunately, any anti-obesity agent was identified based on the in-house drug library.

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TABLE OF CONTENTS

LIST OF ILLUSTRATION AND TABLES

1. Introduction

Diabetes mellitus is a series of metabolic disease characterized by hyperglycemia resulting from the defect in insulin secretion, inadequate tissue response to in insulin, or both [1,2]. Typically, there are two diabetes mellitus:

1. Type 1 Diabetes Mellitus (T1DM)
2. Type 2 Diabetes Mellitus (T2DM)

Type 1 Diabetes Mellitus (T1DM) is a common chronic disease typically developed and diagnosed at an early each (children and teenagers); therefore, it is also called Juvenile diabetes [1]. When patients suffered T1DM, their pancreas (dysfunction) absolutely fail to produce insulin. The mechanism of T1DM results from the immunological destruction of islet β-cells [2]. The onset of T1DM is attributed to both inherited risk and external triggers, such as heredity, diet, and environment [3]. The HLA class II region, a cluster of genes on chromosome 6p21, attribute to 45% genetic susceptibility of T1DM [2,3]. Since β-cells do not produce insulin, insulin administration (insulin injection and insulin pump) is required for the management of T1DM.

Type 2 Diabetes Mellitus (non-insulin dependent diabetes mellitus, T2DM) is more prevalent than other types of diabetes mellitus. It is a long-term metabolic disorder characterized by insulin secretion insufficiency, hyperglycemia, insulin resistance or a combination of them [4]. T2DM has become one of the most critical public health challenges. The International Diabetes Federation (IDF) estimates that more than four million people had diabetes mellitus and caused 1.5 million people died. Approximately, 90% diabetes mellitus patients are affected by T2DM [5]. T2DM has a higher prevalence in middle-income and low-income countries than in developed countries. Unhealthy diet, obesity, physical inactivity, hypertension, increasing age, family history of diabetes mellitus are all risk factors for people to get T2DM. The mechanism of T2DM is very complicated. It can be viewed as a series of pathophysiologic changes, such as β-cell dysfunction, insulin resistance, abnormal lipid metabolism, and chronic inflammation with the consequence of abnormal glucose homeostasis [4,6].

Typically, the management of T2DM is to intake oral and injectable antidiabetic agents with a combination of diet control and appropriate exercise [7].

2. Currently Available Treatment Optional For T2DM

In addition to a healthy diet and appropriate exercise, there are also various treatments, both for oral and injectable, available for the treatment of T2DM. Insulin products and glucagon-like peptide (GLP-1) agonists are available as injectable agents for T2DM management [8]. Besides the injectable agents, there are many oral antidiabetic agents for T2DM, which are easier to access and take compared to injectable agents.

2.1 Dipeptidyl peptidase-4 Inhibitor

Dipeptidyl peptidase-4 inhibitor, also known as DPP-4 inhibitor, is a new oral clinical therapy for T2DM management. The mechanism of DPP-4 inhibitors to reduce glucose levels attribute to their ability to block the enzyme dipeptidyl peptidase-4 (DPP-4) and inhibit incretins degradation such as Glucose-dependent insulinotropic peptide (GIP) and Glucagon-like peptide-1 (GLP-1) [11,12]. Incretins are metabolic hormones in the gut that are secreted from enteroendocrine cells to decrease glucose levels in the blood. GIP and GLP-1 are two different type of incretins which can promote β-cell proliferation and inhibit apoptosis to expand pancreatic β-cell mass [13]. Glucose-dependent insulinotropic peptide (GIP) stimulate insulin secretion to increases incretin activity in the duodenum [14]. GLP-1 induces β-cell to release the hormone insulin in response to glucose level increased while suppressing glucagon, a peptide hormone increases blood glucose levels, secretion [14]. Vildagliptin, Sitagliptin, and Saxagliptin are common DPP-4 inhibitors for T2DM treatment.

2.2 Sodium/Glucose Cotransporter 2 (SGLT-2) Inhibitors

Sodium/Glucose cotransporter-2 (SGLT-2) inhibitors are a type of prescription medicines combined with diet and exercise for T2DM treatment for adults. It reduces glucose levels via its ability to decrease renal glucose reabsorption in the kidney. This process ultimately leads to increased urinary glucose excretion [15]. SGLT-2, encoded by SLC5A2, is a family of proteins that transport glucose across cell membranes against the concentration gradient, which mediate glucose transport across the intestinal lumen and the epithelial cells in the proximal renal tubule [15-17]. SGLT-2 is

over-expressed and over-activated in patients with T2DM, which facilitates glucose reabsorption in the kidney. However, SGLT-2 inhibitors prevent glucose reabsorption in the kidney, remove glucose through urine, and lower plasma glucose levels [18,19]. Six SGLTs have been identified, but only SGLT-1 and SGLT-2 are considered important because of their ability to transport glucose into the cell [20]. SGLT-3 works as a glucose sensor [20,21]. The function of SGLT-4 and SGLT-5 are still unknown [22]. Although both SGLT-1 and SGLT-2 mediate glucose reabsorption in kidney, their affinities and transport capacity are significantly different [17]. SGLT-1 has higher transport capacity and glucose reabsorption ability compared with SGLT-2, but SGLT-1 inhibitors have adverse gastrointestinal effects [17,23,24]. Therefore, SLGT-2 inhibitors are a good candidate for T2DM management.

2.3 Sulfonylureas

Sulfonylureas are a class of oral antidiabetic agents to stimulate β-cell release more insulin in the pancreas [25]. The mechanism of sulfonylureas to decrease glucose level is attributed to their ability to block the potassium channels by targeting the specific site on the cell membrane and subsequently stimulate calcium channels open to cause insulin exocytosis [25]. By binding to the sulfonylureas receptor (SUR) to close potassium channels and depolarize the cell, calcium channels open to trigger exocytosis of insulin [25,26], and therefore increase the secretion of insulin [27]. In addition, it has been proven that sulfonylureas also have extra-pancreatic action. Sulfonylureas could facilitate carbohydrate transportation, enhance skeletal muscle sensitivity to insulin, and increase insulin action on the liver [27,28]. Nowadays, there are three generations of sulfonylureas antidiabetic agents.

2.4 Adenosine 5’-monophosphate (AMP)-activated Protein Kinase (AMPK)

Adenosine 5’-monophosphate (AMP)-activated protein kinase (AMPK) is critical to keep energy metabolism homeostasis [29]. Patients with T2DM, AMPK holds a potential role to reverse the metabolic abnormalities by increasing glucose uptake and facilitating fatty acid catabolism in various

organs, especially in skeletal muscle and the liver [29,30]. AMPK is expressed in many tissues, including liver, brain, and skeletal muscles, which work as a nutrient and energy sensors to keep energy homeostasis in whole-body [31,32]. When cell energy is insufficient, AMPK is activated to stimulate glucose uptake in skeletal muscles, stimulate fatty acid oxidation in adipose tissue, and reduces hepatic glucose production [29]. AMPK suppress fatty acid synthesis, cholesterol synthesis, and glucongeogenesis by inhibiting ATP-consuming pathways. Furthermore, it stimulates ATP-generating processes such as fatty acid oxidation and glycolysis; therefore, restoring overall cellular energy homeostasis [33]. In regulating glucose metabolism, AMPK activation suppresses the expression of two key gluconeogenesis enzymes, PEPK (Phosphoenolpyruvate carboxykinase) and glucose-6-phosphatase, which in turn inhibits gluconeogenesis to improve insulin sensitivity and metabolic health [29,34]

2.5 Peroxisome Proliferator-Activated Receptor (PPARs)

The peroxisome proliferator-activated receptors (PPARs), which include PPAR-α, PPAR-γ, PPAR-ß/δ, are steroid hormone nuclear receptors that worked as transcription factors to regulate specific genes expression [35,36]. It has been proven that PPARs involves in several physiological processes, such as modulation cellular differentiation, development, fatty acid regulation, lipoprotein metabolism, and glucose homeostasis [37,38], therefore, PPARs is a promising therapeutic candidate for metabolic diseases management, especially for the treatment of T2DM. In human beings, PPAR-α is highly expressed in metabolically active tissues, including liver, kidney, brown adipose tissue, vascular smooth muscle cells, and endothelial cells, to enhance insulin sensitivity, fatty acid catabolism, and increase hepatic glucose production [39],40]. PPAR-ß/δ has been detected in all tissues, but it is highly expressed in brain, adipose tissue, pancreatic islets, and skin. The PPAR-ß/δ increase fatty acid oxidation (FAO) in skeletal muscle to improve insulin sensitivity and glucose disposal rate in peripheral tissues; therefore, reducing glucose level [40]. PPAR-γ is abundantly expressed in the intestine, liver, kidney, adipose tissue, and vascular and immune cells [38,40]. It has been reported that PPAR-γ agonists could improve insulin resistance by opposing the TNF-α in

adipocytes [41]. Thiazolidinediones (TZDs) are a type of PPARs agonist to increase insulin sensitivity in both hepatic cells and adipose tissue [42].

2.6 α-Glucosidase Inhibitor

α-Glucosidase inhibitors (AGIs) are a class of oral antidiabetic agents for T2DM management which postpone carbohydrates hydrolyzation in small intestines [43]. α-Glucosidase is a type of carbohydrase distributed widely in microorganisms, plants, and animal tissues [43,44]. Since carbohydrates are the primary source of saccharides people intake from diet, inhibition α-glucosidase could effectively prevent absorption of starch and other carbohydrates [45]. Acarbose is a universal α-glucosidase inhibitor which blocks both α-amylase and α- glucosidase to avoid the intake of starch and sugars in the intestine [45]. In addition to delay carbohydrate hydrolysis, this class of drugs could also facilitate the secretion of incretin hormones and glucagon-like peptide-1 (GLP-1) to reduce the glucose level for patients with T2DM [46].

3. Treatment of Cardiovascular Disease (CVDs) For People With T2DM

Hypertension is a common disease that accompanies T2DM. It has been reported that the incidence of hypertension in diabetics is approximately twice that of people without diabetes mellitus. In addition, recent studies have suggested that hypertensive patients have a higher risk of developing diabetes than people with normal blood pressure [47]. Hypertension, especially in combination with cardiovascular diseases, is the major complication of diabetes mellitus to aggravate the illness, which in turn causes other serious complications including retinopathy with potential blindness, nephropathy probably to lead renal failure, foot ulcers with a high risk of amputation [47]. Therefore, it was recommended to receive hypertension treatment when blood pressure reaches 130/85 mmHg rather than 140/80 for healthy individuals. In addition, there is a tendency for a majority of patients with T2DM represent diabetic retinopathy when the blood pressure is exceeded to 70 mmHg [48]. The pathophysiology mechanism of hypertension in diabetes mellitus is probably attributed to the abnormal sodium level, hyperinsulinemia, and decline of vasodilatory response to insulin in skeletal muscle [48].

Hypertensive treatment of diabetes mellitus, therefore, plays a significant role in complication management and decline the risk of cardiovascular mortality [49]. Evidence from clinical trials has shown that treatment of hypertension in patients with T2DM prevents major clinical complications [49,50]. However, the adverse effect of antihypertensive drugs on insulin sensitivity and diabetic complications should take into account pharmacological therapy [51]. For example, renal disease is a common complication for diabetes mellitus. About 20-30% of patients with diabetes mellitus would develop nephropathy [48]. But some antihypertensive drugs probably aggravate renal diseases. Therefore, the management of hypertension with diabetes mellitus should also be concerned about their therapeutic benefit for diabetic complications. Angiotensin-converting-enzyme inhibitor (ACEI), Thiazide diuretics, α/β-adrenergic receptor inhibitors (α/β-inhibitor), calcium channels blockers (CCB), and angiotensin II receptor blockers (ARBs) are common medication for hypertension and heart failure management for patients with T2DM.

3.1 Angiotensin-Converting-Enzyme (ACE) Inhibitors

Angiotensin-converting-enzyme (ACE) inhibitors are a common pharmaceutical drug for hypertension treatment and congestive heart failure [52]. ACE inhibitors dilate and enlarge the blood vessels to reduce blood pressure and improve the function of a failing heart. Angiotensinogen is a hormone that regulates blood pressure and fluid balance, which belongs to the renin-angiotensin system (RAS) [53]. When kidneys secrete renin into the bloodstream, the renin breaks angiotensinogen down to Angiotensin I. In this process, Angiotensin-converting-enzyme converts Angiotensin I to Angiotensin II in lungs, which is a vasoconstrictive peptide to increase blood pressure [53,54]. Angiotensin II stimulates the adrenal cortex to release aldosterone and constrict the blood vessels. Also, aldosterone increases the reabsorption of water and sodium in the kidney to increase the concentration of sodium in the blood. The combination of blood vessels' constriction and the high sodium concentration in the blood induces hypertension. ACE inhibitors inhibit the angiotensin-converting-enzyme (ACE) to reduce the conversion process to decrease blood pressure. ACE inhibitors also have therapeutic benefits for kidney diseases. ACE inhibitors intervene, or prevent, the development of renal disease, diabetic nephropathy, and diabetic kidney disease [48]. The adverse effects of ACE inhibitors include high blood potassium level, angioedema, dizziness and rash [55].

3.2 Calcium-Channel Blockers (CCBs)

Calcium channel is a selective permeability ion channel to control the calcium concentration inside and outside the cell. Calcium-Channel Blockers (CCBs) reduce the level of calcium by blocking calcium flux into the cell to cause vasodilation, therefore, lowering blood pressure [56]. There are four types of CCBs: dihydropyridine (DHP) CCBs, non-dihydropyridine (non-DHP) CCBs, Benzothiazepine CCBs, and non-selective CCBs [57]. DHP CCBs reduce systemic vascular resistance to induce vasodilators to reduce blood pressure [58]. Non-DHPs tend to inhibit cardiac conduction due to its selective myocardium ability, and it can be used for angina pectoris treatment [58]. Non-DHP CCBs have the ability to reduce the progression of diabetic nephropathy and to reduce proteinuria [59].

Benzothiazepine is a class of CCBs among DHP CCBs and non-DHP CCBs. It is both a cardiac depressant and vasodilator; therefore, it can be used for angina treatment [58]. Non-selective CBBs, including mibefradil, fendiline, and bepridil, are generally used for the treatment of hypertension and angina pectoris. The common adverse effects of CCBs are hypotension, headaches, constipation, and rashes [60].

3.3 Angiotensin-Receptor Blockers (ARBs)

Angiotensin-Receptor blockers (ARBs) are a class of antihypertensive agents, which were developed to overcome defects of ACE inhibitors. Unlike the ACE inhibitors to inhibit angiotensin-Converting-Enzyme, ARBs block the angiotensin II by binding angiotensin II receptors to decrease blood pressure. There are two types of angiotensin II receptors: AGTR1 and AGTR2 [61]. AGTR1, which is widely distributed in blood vessels, heart, and kidney, mediates a variety of signal transduction systems in adults [61]. AGTR2 tends to be more dominant in fetuses and infants [61]. ARBs modulate the renin-angiotensin-aldosterone system (RAAS) by inhibiting Angiotensin II binding to AGTR1 [62]. By blocking the angiotensin II binding to the AGTR1, ARBs induce vasodilation, and decrease reabsorption of water and salt in the kidney, preventing blood vessels and heart fibrosis to decrease blood pressure [62]. Patients are sensitive or suffered serious adverse effects of ACE inhibitors because of the non-specific ability of angiotensin-converting enzyme (ACE), ARBs can be used as alternative antihypertensive agents since ARBs tend to be more selective to the AGTR2 [63]. Furthermore, ARBs play a vital role in the prevention of T2DM, and it has been reported that hypertensive patients with ARBs treatment were 23% lower of the incidence of T2DM [64]. Common side effects of ARBs include hypotension, high potassium level, drowsiness, headache, and diarrhea [65].

3.4 Adrenergic Antagonists

Adrenergic antagonists are a class of drugs that block adrenergic receptors. Adrenergic receptors are a group of G-protein coupled receptors which are targeted by catecholamines,

epinephrine, and norepinephrine to modulate sympathetic nervous response [66]. To respond to stress, the adrenal medulla cells release more catecholamines into the blood to activate adrenergic receptors to trigger a series of biological responses including heart rate increase, heart muscle contraction, blood pressure increase, and sweating [66]. By blocking the activation of adrenergic receptors, adrenergic antagonists suppress sympathetic nervous system or prevent catecholamines secretion. The adrenergic antagonist can be divided into two subtypes: alpha-adrenergic antagonist (α-blocker) and beta-adrenergic antagonist (β-blocker). α-blockers inhibit norepinephrine by binding to smooth muscle receptors to lead vasodilation and reduce blood pressure [67]. There are two types of α-blocker: non-selective α-blocker and selective α-blocker. Non-selective α-blockers are mainly used for the treatment of hypertension, however selective α-blocker are more frequently prescribed for the treatment of benign prostatic hyperplasia (BPH) since they are widely distributed in bladder, neck, and prostate glands [68]. β-Blockers are a class of inhibitors which block the binding sites of norepinephrine and epinephrine on adrenergic beta receptors [69]. It has been proven that β- blockers play a significant role in the treatment of hypertension and cardiac diseases. By decreasing catecholamine levels in the blood, β-blockers inhibit the sympathetic nervous system activation to reduce the cardiac oxygen demand and heartbeat rate to lower heart rate and blood pressure [70]. It has been shown in clinical trials that β-blocker tend to reduce the risk of cardiovascular events and death in post-myocardial infarction patients with diabetes [71].

3.5 Thiazide Diuretics

The thiazide diuretics offer a compelling therapeutics treatment for hypertension, which inhibits sodium reabsorption in the kidney by blocking the Sodium-Chloride cotransporter (NCC) [72]. By inhibiting the Sodium-Chloride cotransporter, the reabsorption of sodium and chlorine is decreased which increases the urine output [72]. The extracellular fluid and plasma volume are decreased due to water loss from urine, which triggers venous return decreasing, renin release increasing, cardiac output, and blood pressure decreasing [72]. For the chronical treatment of thiazide diuretics, the mechanism of thiazide seems different. During long-term treatment, thiazide causes vasodilation by

reducing the total peripheral resistance (TPR); however, the mechanism is still not clearly understood [72]. The common adverse effects of thiazide diuretics include hypokalemia, hyperuricemia, hypercalcemia, new-onset diabetes [72]. Among those side effects, hypokalemia is the primary cause of glucose resistance which leads to new onset diabetes mellitus. It has been reported that the hypokalemia of thiazide diuretics response is 1.8% to 3.5% of the incidence of new-onset diabetes mellitus increase [73]. Therefore, thiazide diuretics should be prescribed carefully especially for patients with diabetes.

4. Herbal Remedies for Diabetes Mellitus

With the increasing severity of T2DM, herbal remedies are playing a significant role in the health service system. Herbal remedies have been widely used to treat various diseases since ancient times. The bioactive substances contained in herbs remedies have proven therapeutic efficacy with lower adverse effects than other pharmaceuticals. Many people who suffer from diabetes in developing countries choose to take herbal remedies since it is more affordable and accessible than prescription medications. In this thesis, I investigated three traditional remedies for the T2DM management.

Khaya Senegalensis, (11L) which is a popular medicinal plant, belongs to Meliaceas family and is native to Africa. *Khaya Senegalensis* is a tree with shiny leaves and grows a minimum of 25 meters tall or morer with exfoliated bark [74]. Based on the phytochemical screening for 11L, it contains anti-microbial agents [74], anti-cancer agents/properties [75], and anti-oxidant agents [76]. The extraction of the stem, bark, and seed was traditionally used for the treatment of malaria, jaundice, edema, and headache [77]. A recent study has shown the ethanolic extract of the root has the ability to inhibit α-glucosidase and α-amylase to decrease glucose levels in the blood [78].

Anacardium Occidentale (12M), also known as cashew, is a tropical evergreen tree that was originally grown in Central and South America [79]. It is a valuable cash crop in the Americas and the West Indies [80]. Cashew is a good source of vitamin A and vitamin C [79]. Cashew nut is a good source of oil, and Cashew apple is edible [81]. The biological activities of cashew have been reported to have the anti-antioxidant capacity [82], antiviral [83], and anti-inflammatory activities [84].

Moringa Oleifera Lam (13M) is one of the best known tropical plants with high nutritive and medicinal value distributed in many countries of the tropics and subtropics [84,85]. Moringa leaves contain various natural antioxidants includes β-carotene, sterols, vitamin C, glycosides, alkaloids and flavonoids [86]. Antihypertensive compounds, thiocarbamate and isothiocyanate glycosides, have been isolated from the acetate phase of the ethanolic extract of Moringa seeds [87]. Other medicinal uses and pharmacological properties for *Moringa Ofeifera* such as a diuretic, lowering cholesterol,

anti-bacterial, anti-tumor and anticancer activities have been reported [87].

5. Materials And Methods

5.1 Plant Sample Collection

The seeds of 11L, 12M, and 13N were collected at different sites to reduce experimental error due to the difference in growth conditions, such as weather, soil quality, and temperature. The seeds were then stored and transported in moisture-free conditions.

5.2 Compound Extraction

Methanol +1% Acetic Acid was used to extract the seeds, which have been proven to have the greatest ability to reduce blood glucose levels from a previous study in our lab. The seeds were then dried and crushed before extraction. After adding the solvent for extraction, the mixture was shaken for 5 days at room temperature on a VWR Standard Shaker set at Speed 3. Using cotton and a funnel to filter the mixture, and the filtrate was air-dried at room temperature [Fig.1].

5.3 HPLC/MS Data Acquisition

HPLC/MS data acquisition and data analysis were done as according to well established methods in the Kotchoni Lab and described previously [88].

5.4 Data Analysis, Database Search, and In-house Library

For compound identification, the proprietary integrated Bruker software was used according to the manufacturer recommendation. For In-house library repository, public databases such as PubChem (https://pubchem.ncbi.nim.nih.gov/), DrugBank (https://www.drugbank.ca), KEGG (Kyoto Encyclopedia of Genes and Genomes) and ChemSpider (chemspider.com) were collected to construct the in-house Drugs Library repository and to be used subsequently to check anti-diabetic, anti-hypertensive, and anti-obesity agents. Extraction ion chromatogram (EIC) of each compound (drug) in our library was performed to identify the presence or absence of these drugs in our sample base peak chromatogram (BPC), respectively. The accuracy of the EIC of the drug/compound to be identified

was performed using the integrated Bruker proprietary software (DataAnalysis 4.2, SmartFormula Manual, CompoundCrowler) according to the manufacturer recommendation. A Heatmap was then created based on the mean intensity of three replicate runs of the samples, respectively. A Venn diagram was also created to show the common compounds (drugs) in extraction in 11L 12M and 13N.

6. Results

From the HPLC/MS data acquisition and data analysis, a total of 186 compounds were dissected and identified. A Venn diagram was also created to show the common compounds (drugs) in extraction in *Khaya Senegalensis* (11L), *Anacardium Occidentale* (12M), and *Moringa Oleifera* Lam (13N), respectively [Fig.2]. The heat map based on the mean relative intensity, to measure the detector response, of those 186 compounds was constructed [Fig.3-6]. There are 89 compounds are dissected and identified in the seed extraction of three plants. 6-[2-[[2-[(2S)-2-cyanopyrrolidin-1-yl]- 2-oxoethyl]amino]ethylamino]pyridine-3-carbonitrile ($C_{15}H_{18}N_6O$) and 2-ethyl-4-[[4-[2-(2H-tetrazol -5-yl)phenyl]phenyl] methoxy]-5,6,7,8- tetrahydroquinoline ($C_{25}H_{25}N_5O$) are two exclusive compounds for Khaya Senegalensis (11L) and Moringa Oleifera Lam (13N), respectively.

Several plants' secondary metabolites were found, such as 1-aminocyclopropane-1-carboxylic acid ($C_4H_7NO_2$) found in the seed extraction of 11L, 12M, and 13N. (1S)-1-[(3-hydroxy-4-methoxyphenyl)methyl]-6-methoxy-2-methyl-3,4-dihydro-1H-isoquinolin-7-ol ($C_{19}H_{23}NO_4$), and 4-(2-Aminoethyl)phenol ($C_8H_{11}NO$) are two secondary metabolites were identified in 12M and 13N. Some secondary metabolites have pharmacological activities. For example, 1,3-dimethyl-7H-purine -2,6-dione ($C_7H_8N_4O_2$) is the secondary metabolites identified in 11L, 12M, and 13N, which has the diuretic and vasodilator action. Some vitamins are also identified in all three plants extraction, such as pyridine-3-carboxylic acid ($C_6H_5NO_2$), which is a water-soluble vitamin belongs to the vitamin B family to use as an antihyperlipidemic agent to reduce LDL cholesterol, triglycerides and HDL cholesterol [89]. 4,5-bis(hydroxymethyl)-2-methylpyridin-3-ol (Vitamin B6) ($C_8H_{11}NO_3$) with the potency to lower blood pressure and cholesterol level was dissected and identified in the seed extraction of 12M and 13N. In addition, some identified compounds have anti-cancer and anti-viral effects, such as 1-methyl-3-[4-[[methyl(nitroso)carbamoyl] amino]butyl]-1-nitrosourea ($C_8H_{16}N_6O_4$), which dissected and identified in 11L, 12M, and 13N.

Chronic inflammation is one of the pathophysiological mechanism to cause diabetes mellitus. Inflammations would decrease β-cell insulin secretion and increase insulin resistance [90]. Islet cell

and adipocyte inflammation are already recognized in the pathogenesis of new-onset and worsen the condition of T2DM [91]. Furthermore, adipocyte inflammation also participated in atherosclerosis development which restricted and blocked the blood supply to cause other cardiovascular diseases [91]. And oxidative stress also causes inflammation. Therefore, anti-inflammatory and anti-oxidative therapies are a new compelling treatment of T2DM, diabetic complications, and cardiovascular diseases. Some anti-inflammatory and antioxidant compounds were dissected and identified from the chromatogram profile such as benzene-1,2,3-triol ($C_6H_5O_3$) [90], S-[2-[[(2R)-2-acetamido -3-sulfanylpropanoyl]amino]ethyl] 2-methylpropanethioate ($C_{11}H_{20}N_2O_3S_2$), and 1-hydroxy-2,2,6,6 -tetramethylpiperidin-4-ol ($C_9H_{19}NO_2$). And among all compounds, five antidiabetic agents and three antihypertensive agents were dissected and identified.

6.1 Antidiabetic Agents Identification

NVP-DPP728 [Fig.7] is a highly selective, oral DPP-inhibitor found in 11L developed by Novartis, which unfortunately discontinued in phase II trials for the treatment of T2DM [92]. By inhibiting the dipeptidyl peptidase-IV enzyme (DPP-4) and blocking incretin hormones degradation such as the glucose-dependent insulinotropic polypeptide(GIP) and glucagon-like peptide-1 (GLP-1), NVP-DPP728 increases insulin secretion and decreases glucagon release, thereby, decreasing glucose levels in the blood. It has been reported the treatment of NVP- DPP728 reduced plasma glucagon levels in cats [93]. Another clinical study also showed that administration of NVP-DPP728 increases the prandial intact GLP-1 level and reduces glucose exposure in humans compared with the placebo treatment [92]. Consequently, NVP-DPP728 is a compelling antidiabetic agent for the treatment of T2DM.

Voglibose [Fig.8-9]. is an α-glucosidase inhibitor found in 11L and 12M which can be used for lowering post-prandial blood glucose levels in people with diabetes mellitus [94]. It is an oral-diabetic drug used for T2DM by preventing the digestion of complex carbohydrate. Voglibose was approved in Japan in 1994 for the treatment of diabetes mellitus [95] By inhibiting α-glucosidase in the small intestine, Voglibose delays starch and disaccharides hydrolysis to glucose and prevents

glucose absorption by inhibiting carbohydrate digestion to reduces glucose level [95]. Voglibose also facilitates the secretion of GLP-1 to stimulate insulin secretion and decrease insulin resistance [95]. Since the post-prandial hyperglycemia is the primary cause of diabetic complications (including macro-vascular and microvascular complications), the post-prandial antidiabetic agents, such as Voglibose, could significantly decrease of the risk of the development of cardiovascular diseases and hypertension [95,96]. The main adverse effect of Voglibose includes diarrhea, nausea, hepatitis, vomiting, and dizziness [95].

Acetohexamide [Fig.10-11]. is a type of antidiabetic agent that belongs to the sulfonylureas family found in 11L and 12M. Acetohexamide is first-generation oral sulfonylurea [96]. It reduces blood glucose level by stimulating the pancreatic β-cells to secrete more insulin and enhance insulin sensitivity of the body. Acetohexamide has been discontinued in the US market. When the concentration of glucose increases, the ATP-sensitive potassium channel is closed which lead to depolarization of the cell due to increasing concentration of potassium inside the cell. In response to the depolarization of the cell, the Voltage-Gated calcium channel is opened, calcium is influx into the cell to induce insulin secretion [96]. Acetohexamide causes ATP-sensitive channel closure to enhance insulin secretion. Sulfonylureas also decrease hepatic hormone levels and enhance insulin levels [96]. As an antidiabetic agent, Sulfonylurea usually intake combines with metformin, a biguanide which increases insulin sensitivity by improving hepatic insulin responses, for T2DM management, which decreased the risk of mortality of cardiovascular disease [97]. The main adverse effect of Acetohexamide is hypoglycemia because of the excessive insulin level [96,97].

Acadesine [Fig.12], and A-769662 [Fig.13] are two activators of AMP-activated protein kinase (AMPK) found in 12M. A-769662 reduces glucose levels in the blood by stimulating AMPK release and inhibiting fatty acid synthesis in mice [98]. It is a feasible candidate for the treatment of the T2DM and metabolic syndrome. Acadesine is also used for the treatment of impaired glucose tolerance and insulin resistance in T1DM and T2DM [99]. However, the poor oral bioavailability of Acadesine limits its application as an oral antidiabetic agent. Acadesine is also used for the treatment of chronic lymphocytic leukemia, but the study was discontinued in phased III [100]. AMPK is a

major energy sensor in the cell which is activated during energy depilation [101]. AMPK regulate AMP: ATP ratio to keep metabolic homeostasis [102]. The AMPK activators are capable of enhancing glucose uptake and utilization, fatty acid oxidation, and mitochondrial biogenesis; meanwhile, AMPK activators decrease cholesterol synthesis, lipid synthesis and hepatic lipogenesis [102].

6.2 Antihypertensive Agents Identification

Carteolol [Fig.14] and Nipradilol [Fig.15] are two β-adrenergic antagonists found in 12M which are used as an anti-arrhythmia agent, anti-angina agent, and antihypertensive agent. Carteolol is also used for the treatment of open-angle glaucoma [103]. Carteolol is the first generation, non-selective, β-blocker which block both β-1 and β-2 adrenergic receptor. Carteolol is typically used to reduce intraocular pressure and glaucoma management [103]. Nipradilol is another β-blocker found in 12M, which was developed in Japan. Nipradilol can inhibit both β-1 and β-2 adrenergic receptors [104]. Nipradilol is also a nitrovasodilator, which induces vasodilation by releasing NO, an endothelium-derived relaxing factor (EDRF) [104].

ZD-6888[Fig.16] is an ARB found in 13N. ZD-6888 was in phase I clinical trial by AstraZeneca for the treatment of hypertension. However, this research has been discontinued. It has been reported that ZD-6888 blocks the Angiotensin II binding site to inhibit renin-angiotensin-aldosterone system (RAAS) to treat cardiovascular disease [105,106], diabetes mellitus, obesity and metabolic syndrome [106].

7. Discussion

The demand for novel, accessible and cheap antidiabetic and antihypertensive agents has increased following the increased global prevalence of diabetes. This research aims to identify antidiabetic and anti-hypertensive agents from three typical tropics plants：*Khaya Senegalensis* (11L), *Anacardium Occidentale* (12M), and *Moringa oleifera* (13N), which are traditionally used as tea and herbal remedies for the treatment of T2DM in developing countries. Identification of antidiabetic and antihypertensive compounds provides an excellent method to guarantee their safety when they are used as herbal remedies. Those plants could become potential synthesis resources for anti-diabetic and anti-hypertensive drugs. Besides, those three plants are more accessible and cheaper if they used as herbal remedies and food consumption for people in tropics and developing countries.

The in-house drug library was constructed and collected 92 antidiabetic agents through various databases, such as PubChem, Drug Bank, KEGG and ChemSpider. To identify the presence or absence of those compounds (drugs), extraction ion chromatogram (EIC) was performed in samples base peak chromatogram (BPC). Four antidiabetic agents were identified.

Since hypertension is a significant complication of T2DM, and chronic hypertension also attributes to new-onset T2DM. The in-house drug library for antihypertensive agents was also constructed, and 170 antihypertensive agents were collected. Nipradilol and Carteolol are two β-blockers found in 12M, which could be used as anti-hypertensive, but they are more typically used for the open-angle glaucoma treatment. And glaucoma is twice as prevalent in people with diabetes [107]. ZD-6888 is an ARB for hypertension treatment found in 13N.

Obesity is attributed to various chronic diseases such as cardiovascular disease, cancer, and T2DM, and more than 80% of patients with T2DM are overweight or obese [108]. Therefore, the treatment of obesity is crucial for the prevention of the new onset of diabetes mellitus, complications of diabetes mellitus, and cardiovascular disease [108]. Thirty-four anti-obesity agents, which used for the T2DM management, were collected for the anti-obesity in-house drug library; however, none of them were found in the chromatogram profile. But an anti-obesity agent, (2S,3S)-3,4-dimethyl-2-phenylmorpholine (C12H17NO), was dissected and identified in 11L, 12M and 13N for previously analysis. In addition, some

secondary metabolites with anti-inflammatory and anti-oxidant action were also dissected and identified. Recent research suggests that chronic inflammation and oxidation may play a critical role in the development of T2DM.

And secondary metabolites with other pharmacological efficacy were also investigated and identified of the three plants in other publications. Two limonoids with anticancer and antiproliferative efficacy were isolated from the methanol extract of 11L [75]. Compounds with antimicrobial activity [109], antioxidant capacity [82], and antitumor action [110] were identified in 12M. Some secondary metabolites with anti-dyslipidemic, antioxidant, antiulcer, and analgesic were identified in the extraction of 13N [111]. Therefore, 11L, 12M, and 13N are potential candidates for antidiabetic, antihypertensive, and anti-obesity drugs sources, and they are good choices for food consumption since the variety of secondary metabolites contained.

8.1 In-House Drug Library

8.1 Dipeptidyl peptidase-4 Inhibitor

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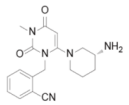
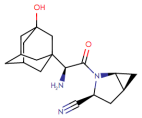
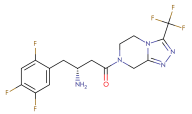
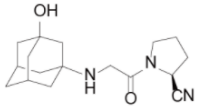
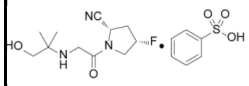
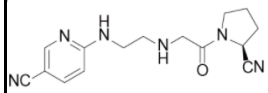
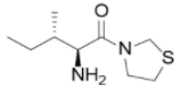
	$C_{18}H_{21}N_5O_2$	Alogliptin	CAS No.850649-61-5 CID:11450633 KEGG: D06553	339.3916	DPP-4 Inhibitor	Approved	T2DM
	$C_{18}H_{25}N_3O_2$	Saxagliptin	CAS No.361442-04-8 CID:11243969 KEGG: D08996	315.41	DPP-4 Inhibitor	Approved	T2DM
	$C_{16}H_{15}F_6N_5O$	Sitagliptin	CAS No.486460-32-6 CID:4369359	407.3136	DPP-4 Inhibitor	Approved	T2DM
	$C_{17}H_{25}N_3O_2$	Vildagliptin	CAS No.274901-16-5 CID:6918537 KEGG: D07080	303.3993	DPP-4 Inhibitor	Approved	T2DM
	$C_{17}H_{24}FN_3O_5S$	TS-021	CAS No.667865-69-2 CID:9865778	401.45	DPP-4 Inhibitor	Phase I discontinued	T2DM
	$C_{15}H_{18}N_6O$	NVP-DPP728	CAS No.207556-62-5	298.35	DPP-4 Inhibitor	Phase II discontinued	T2DM
	$C_9H_{18}N_2OS$	P32/98	CAS No.136259-20-6 CID:6918464	202.32	DPP-4 Inhibitor	Phase II discontinued	T2DM

Anti-diabetic Agent (DPP-4 Inhibitor)							
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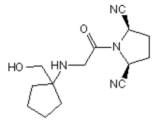
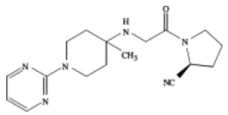
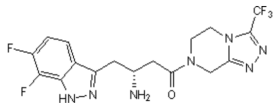
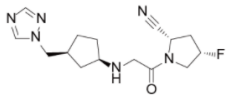
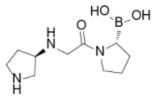
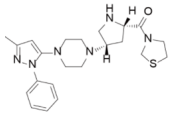
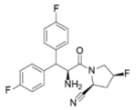
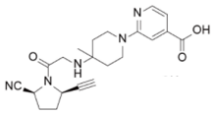
	$C_{14}H_{21}N_4O_2$	DP-893	CAS No. 866396-70-5 CID:11381415	312.798	DPP-4 Inhibitor	Unknown	Research
	$C_{17}H_{24}N_6O$	K-579	CAS No.440100-64-1 CID:9818824	328.41	DPP-4 Inhibitor	Unknown	Research
	$C_{17}H_{16}F_5N_7O$	PK-44	CAS No.1017682-66-4 CID:90488917	429,35	DPP-4 Inhibitor	Unknown	Research
	$C_{15}H_{21}FN_6O$	Melogliptin	CAS No.868771-57-7 CID:11623906	320.372	DPP-4 Inhibitor	Unknown	Research
	$C_{10}H_{20}BN_3O_3$	Dutogliptin	CAS No.852329-66-9 CID:11253490	241.1	DPP-4 Inhibitor	Phase III discontinued	T2DM
	$C_{22}H_{30}N_6OS$	Teneligliptin	CAS No.760937-92-6 CID:11949652	426.583	DPP-4 Inhibitor	Approved	T2DM
	$C_{20}H_{18}F_3N_3O$	Denagliptin	CAS No.483369-58-0 CID:9887755	373.379	DPP-4 Inhibitor	Phase III discontinued	T2DM
	$C_{21}H_{25}N_5O_3$	ABT-279	CAS No.676559-84-3 CID:16049769	395.463	DPP-4 Inhibitor	Phase I discontinued	T2DM

Anti-diabetic Agent (DPP-4 Inhibitor)							
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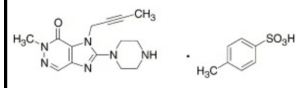
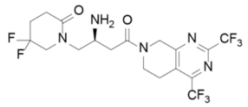
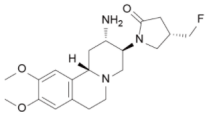
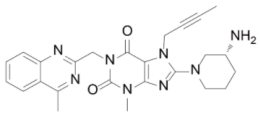
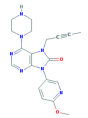
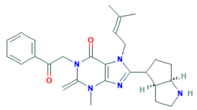
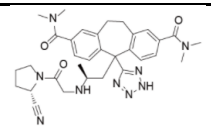
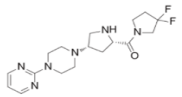
	$C_{21}H_{26}N_6O_4S$	E-3024	CAS No.635722-43-9 CID:11992144	458.537	DPP-4 Inhibitor	Unknown	Research
	$C_{18}H_{19}F_8N_5O_2$	Gemigliptin	CAS No.911637-19-9 CID:11953153	489.37	DPP-4 Inhibitor	Approved	T2DM
	$C_{20}H_{28}FN_3O_3$	Carmegliptin	CAS No.813452-18-5 CID: 11417567	377.453	DPP-4 Inhibitor	Phase II discontinued	T2DM
	$C_{25}H_{28}N_8O_2$	Linagliptin	CAS No.668270-12-0 CID:10096344 KEGG: D09566	472.5422	DPP-4 Inhibitor	Approved	T2DM
	$C_{19}H_{21}N_7O_2$	ER-319711	CID:15605089	379.424	DPP-4 Inhibitor	Unknown	Research
	$C_{27}H_{33}N_5O_2$	SSR-162369	CID:56603733	459.594	DPP-4 Inhibitor	Phase I discontinued	T2DM
	$C_{32}H_{39}N_9O_3$	ALS-2-0426	CAS No.913978-37-7 CID:597.724	597.724	DPP-4 Inhibitor	Phase II discontinued	T2DM
	$C_{17}H_{24}F_2N_6O$	Gosogliptin	CAS No.869490-23-3 CID:11516136	366.417	DPP-4 Inhibitor	NDA Filing	T2DM

Anti-diabetic Agent (DPP-4 Inhibitor)							
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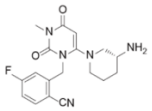
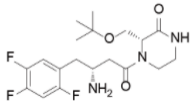
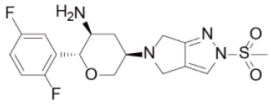
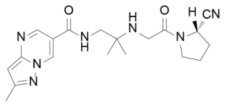
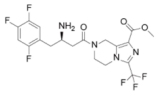
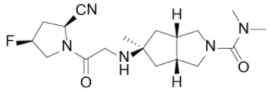
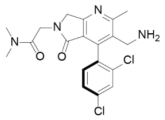
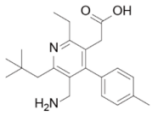
	$C_{18}H_{20}FN_5O_2$	Trelagliptin	CAS No. 865759-25-7 CID:15983988	357.389	DPP-4 Inhibitor	Approved	T2DM
	$C_{19}H_{26}F_3N_3O_3$	Evogliptin	CAS No.1222102-29-5 CID:25022354	401.43	DPP-4 Inhibitor	Approved	T2DM
	$C_{17}H_{20}F_2N_4O_3S$	Omarigliptin	CAS No.1226781-44-7 CID:46209133 KEGG: D10317	398.43	DPP-4 Inhibitor	Approved	T2DM & Chronic Renal Insufficiency
	$C_{19}H_{25}N_7O_2$	Anagliptin	CAS No.739366-20-2	383.456	DPP-4 Inhibitor	Approved	LDL Cholesterol & T2DM
	$C_{19}H_{18}F_6N_4O_3$	Retagliptin	CAS No.1174122-54-3 CID:44193830	464.368	DPP-4 Inhibitor	NDA Filing	T2DM
	$C_{18}H_{28}FN_5O_2$	Besigliptin	CAS No.1177459-85-6	365.453	DPP-4 Inhibitor	Phase II discontinued	T2DM
	$C_{19}H_{20}Cl_2N_4O_2$	BMS-767778	CAS No.915729-95-2	407.29	DPP-4 Inhibitor	Phase II discontinued	T2DM
	$C_{22}H_{30}N_2O_2$	TAK-100	CAS No.907609-33-0 CID:53326686	354.492	DPP-4 Inhibitor	Phase I discontinued	T2DM

Anti-diabetic Agent (DPP-4 Inhibitor)							
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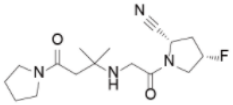
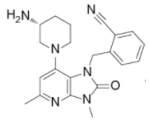
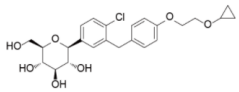
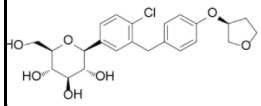
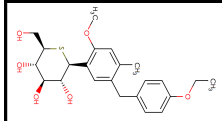
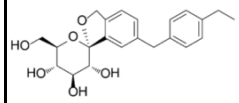
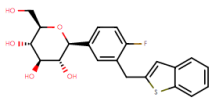
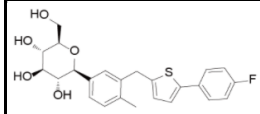
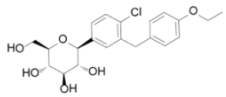
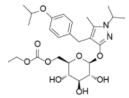
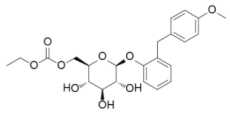
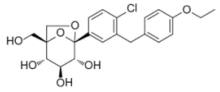
	$C_{16}H_{25}FN_4O_2$	DBPR-108	CAS No.1186426-66-3 CID:44201003	324.4	DPP-4 Inhibitor	Phase II active	T2DM
	$C_{21}H_{24}N_6O$	Imigliptin	CAS No.1314944-07-4 CID:53311070	376.464	DPP-4 Inhibitor	Phase II active	T2DM

Total: 33

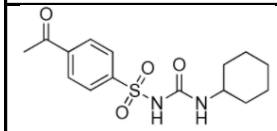
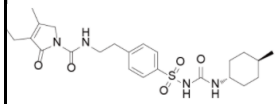
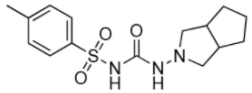
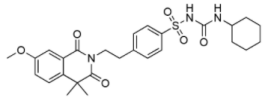
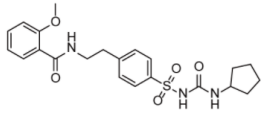
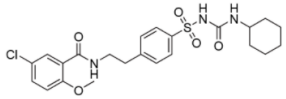
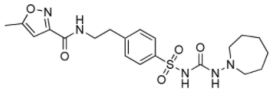
8.2 Sodium/Glucose Cotransporter 2 (SGLT-2) Inhibitors

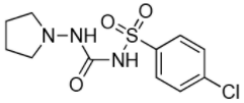
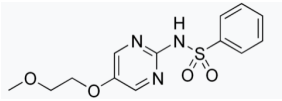
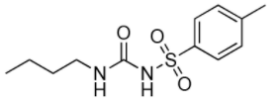
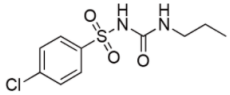
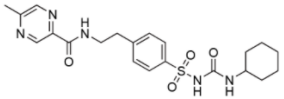
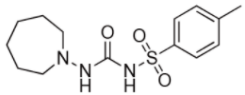
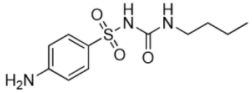
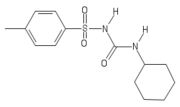
Anti-diabetic Agent (SGLT-2 Inhibitor)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{24}H_{29}ClO_7$	Bexagliflozin	CAS No.1118567-05-7 CID:25195624	464.94	SGLT-2 Inhibitor	Phase III active	T2DM
	$C_{23}H_{27}ClO_7$	Empagliflozin	CAS No.864070-44-0 CID:11949646 KEGG: D10459	450.91	SGLT-2 Inhibitor	Approved	T2DM
	$C_{23}H_{30}O_6S$	Luseogliflozin	CAS No.898537-18-3 CID:11988953	434.55	SGLT-2 Inhibitor	Investigation	T2DM
	$C_{22}H_{26}O_6$	Tofogliflozin	CAS No.903565-83-3 CID:46908929 KEGG: D09978	386.444	SGLT-2 Inhibitor	Approved	T2DM
	$C_{21}H_{21}FO_5S$	Ipragliflozin	CAS No.761423-87-4 CID:10453870	404.45	SGLT-2 Inhibitor	Approved	T2DM
	$C_{24}H_{25}FO_5S$	Canagliflozin	CAS No.842133-18-0 CID:24812758	444.516	SGLT-2 Inhibitor	Approved	T2DM
	$C_{21}H_{25}ClO_6$	Dapagliflozin	CAS No.461432-26-8 CID:9887712 KEGG:D08897	408.873	SGLT-2 Inhibitor	Approved	T2DM

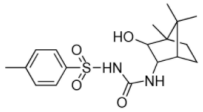
Anti-diabetic Agent (SGLT-2 Inhibitor)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{26}H_{38}N_2O_9$	Remogliflozin etabonate	CAS No.442210-24-3 CID:9871420 KEGG: D10055	522.595	SGLT-2 Inhibitor	Phase II active	T2DM
	$C_{23}H_{28}O_9$	Sergliflozin	CAS No.408504-26-7 CID:9824918	448.468	SGLT-2 Inhibitor	Phase II Discontinued	Anti-hyperglycemic
	$C_{22}H_{25}ClO_7$	Ertugliflozin	CAS No.1210344-57-2 CID:44814423	436.88	SGLT-2 Inhibitor	Approved	T2DM

Total: 10

8.3 Sulfonylureas

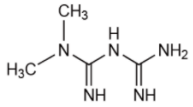
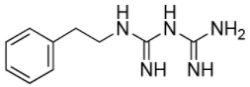
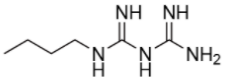
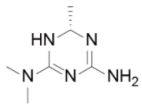
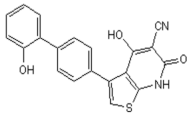
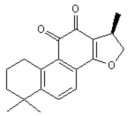
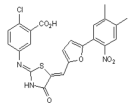
Anti-diabetic Agent (Sulfonylureas)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{15}H_{20}N_2O_4S$	Acetohexamide	CAS No.968-81-0 CID:1989 KEGG: D00219	324.395	Sulfonamide type sulfonylurea receptor agonist	Withdrawn	T2DM
	$C_{24}H_{34}N_4O_5S$	Glimepiride	CAS NO.93479-97-1 CID:3476 KEGG: D00593	490.617	Sufonylurea receptor modulators	Approved	T2DM
	$C_{15}H_{21}N_3O_3S$	Gliclazide	CAS No.21187-98-4 CID:3475 KEGG: D01599	323.411	Sulfonylurea receptor agonist	Approved	T2DM
	$C_{27}H_{33}N_3O_6S$	Gliquidone	CAS No.33342-05-1 CID:91610 KEGG: D02430	527.632	ATP-dependent K^+ (KATP) Channel blocker	Approved	T2DM
	$C_{22}H_{27}N_3O_5S$	Glisentide	CAS NO.32797-92-5 CID:65779	445.534	Sulfonamide type sulfonylurea receptor agonist	Approved	T2DM
	$C_{23}H_{28}ClN_3O_5S$	Glibenclamide (Glyburide)	CAS No.10238-21-8 CID:3488 KEGG: D00336	494.004	Sulfonylurea	Approved	T2DM
	$C_{20}H_{27}N_5O_5S$	Glisoxepide	CAS No.25046-79-1 CID:32778 KEGG: D07118	449.524	Non-selective K^+ (ATP) channel blocker	Approved	T2DM

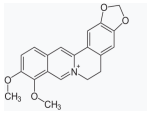
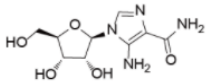
Anti-diabetic Agent (Sulfonylureas)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{11}H_{14}ClN_3O_3S$	Glyclopyramide	CAS No.631-27-6 CID:71793 KEGG: D01799	303.761	Sulfonamide type sulfonylurea receptor agonist	Approved	T2DM
	$C_{13}H_{15}N_3O_4S$	Glycodiazine	CAS No.339-44-6 CID:9565	309.341	Sufapyrimidine derivatve	Approved	T2DM
	$C_{12}H_{18}N_2O_3S$	Tolbutamide	CAS No.64-77-7 CID:5505 KEGG: D00380	270.347	Sulfonylurea receptor 1 inhibitor	Approved	T2DM
	$C_{10}H_{13}ClN_2O_3S$	Chlorpropamide	CAS No.94-20-2 CID:2727 KEGG: D00271	276.74	Sulfonylurea receptor agonist	Approved	T2DM
	$C_{21}H_{27}N_5O_4S$	Glipizide	CAS No.29094-61-9 CID:3478 KEGG: D00335	445.535	Sulfonylurea	Approved	T2DM
	$C_{14}H_{21}N_3O_3S$	Tolazamide	CAS No.1156-19-0 CID:5503 KEGG: D00379	311.4	Sulfonylurea receptor agonist	Approved	T2DM
	$C_{11}H_{17}N_3O_3S$	Carbutamide	CAS No.339-43-5 CID:9564	271.335	Sulfonamide type sulfonylurea receptor agonists	Withdrawn	T2DM
	$C_{14}H_{20}N_2O_3S$	Glycyclamide	CID:12628	296.385	Sulfonylurea	Unknown	Research

Anti-diabetic Agent (Sulfonylureas)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{18}H_{26}N_2O_4S$	Glibornuride	CAS No.26944-48-9 CID:12818200 KEGG: D02427	366.476	Sulfonamide type sulfonylurea receptor agonist	Withdrawn	T2DM

Total: 16

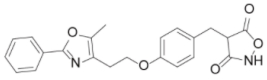
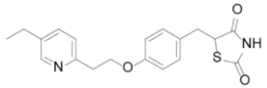
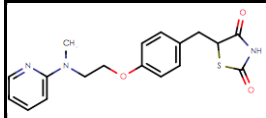
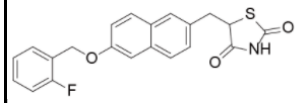
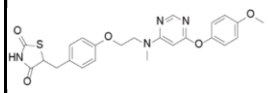
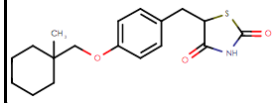
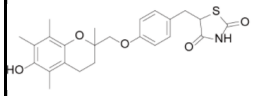
8.4 Adenosine 5'-monophosphate (AMP)-activated Protein Kinase

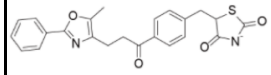
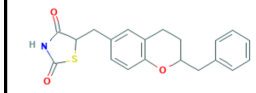
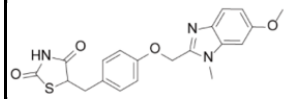
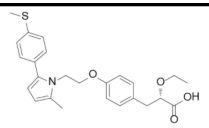
Anti-diabetic Agent (AMP-Activated Protein Kinase (AMPK) Activators)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_4H_{11}N_5$	Metformin	CAS No.657-24-9 CID:4091 KEGG: D04966	129.1636	AMPK Activator	Approved	T2DM
	$C_{10}H_{15}N_5$	Phenformin	CAS No.114-86-3 CID:8249 KEGG: D0835	205.2596	AMPK Activator	Withdrawn	T2DM
	$C_6H_{15}N_5$	Buformin	CAS No.692-13-7 CID:2468 KEGG: D00595	157.2168	AMPK Activator	Withdrawn	T2DM
	$C_6H_{13}N_5$	Meglimin	CAS No.775351-65-0 CID:24812808	155.205	AMPK Activator	Phase III active	T2DM
	$C_{20}H_{12}N_2O_3S$	A-769662	CAS No.844499-71-4 CID:54708532	360.39	AMPK Activator	Unknow	Research
	$C_{19}H_{20}O_3$	Cryptotanshinone	CAS No.35825-57-1 CID:160254	296.366	AMPK Activator	Unknow	Research
	$C_{23}H_{16}ClN_3O_6S$	PT 1	CAS No.331002-70-1 CID:5753734	497.906	AMPK Activator	Unknow	Research

Anti-diabetic Agent (AMP-activated protein kinase (AMPK) Activators)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{20}H_{18}NO_4$	Berberine	CAS No.2086-83-1 CID:2353	336.367	AMPK Activator	Unknow	Research
	$C_9H_{14}N_4O_5$	Acadesine	CAS No.2627-69-2 CID:17513 KEGG: D02742	258.234	AMPK Activator	Phase III discontinued	Leukemia & T2DM

Total: 9

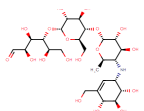
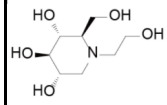
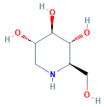
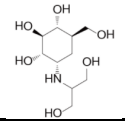
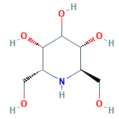
8.5 Peroxisome Proliferator-Activated Receptor (PPARs)

Anti-diabetic Agent (PPARα&PPARγ Agonist)							
Structure	Formular	Name	Number	M.W.	MOA	Status	Indication
	$C_{22}H_{20}N_2O_5$	Reglitazar	CAS No. 170861-63-9 CID:154000	392.411	PPARα Agonist & PPARγ Agonist	Phase II discontinued	T2DM
	$C_{19}H_{20}N_2O_3S$	Pioglitazone	CAS No.111025-46-8 CID:4829 KEGG:D08378	356.439	PPARγ Agonist	Approved	T2DM
	$C_{18}H_{19}N_3O_3S$	Rosiglitazone	CAS No.122320-73-4 CID:77999 KEGG:D00596	357.427	PPARγ Agonist	Approved	T2DM
	$C_{21}H_{16}FNO_3S$	Netoglitazone	CAS No.161600-01-7 CID:204109 KEGG:D05150	381.421	PPARα Agonist & PPARγ Agonist	Phase II discontinued	T2DM
	$C_{24}H_{24}N_4O_5S$	Lobeglitazone	CAS No.607723-33-1 CID:9826451	480.539	PPARα Agonist	Clinical Trials	T2DM
	$C_{18}H_{23}NO_3S$	Ciglitazone	CAS No.74772-77-3 CID:2750 KEGG:D03493	333.446	PPARγ Agonist	Phase II discontinued	T2DM
	$C_{24}H_{27}NO_5S$	Troglitazone	CAS NO.97322-87-7 CID:5591 KEGG:D00395	441.542	PPARα Agonist & PPARγ Agonist	Withdrawn	T2DM

Anti-diabetic Agent (PPARα&PPARγ Agonist)							
Structure	Formular	Name	Number	M.W.	MOA	Status	Indication
	$C_{23}H_{20}N_2O_4S$	Darglitazone	CAS No.141200-24-0 CID:60870	420.483	PPARγ Agonist	Phase I discontinued	T2DM
	$C_{20}H_{19}NO_3S$	Englitazone	CAS No.109229-58-5 CID:60303	353.436	PPARγ Agonist	Unknown	T2DM
	$C_{20}H_{19}N_3O_4S$	Rivoglitazone	CAS No.185428-18-6 CID:3055168	397.449	PPARγ Agonist	Phase Iii discontinued	T2DM
	$C_{25}H_{29}NO_4S$	Saroglitazar	CAS No.495399-09-2 CID:60151560	439.57	PPAR Agonist	Approved	Diabetic-dyslipidemia

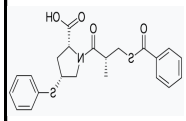
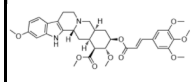
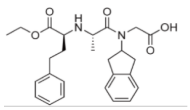
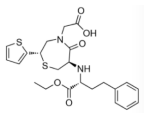
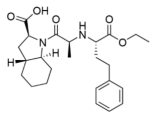
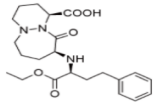
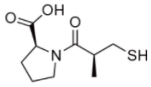
Total: 11

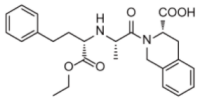
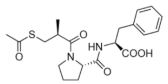
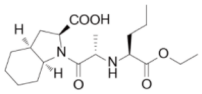
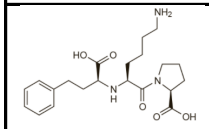
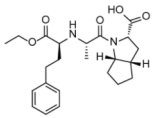
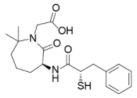
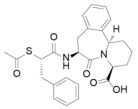
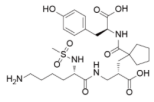
8.6 α-Glucosidase Inhibitor

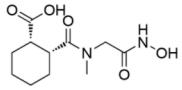
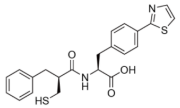
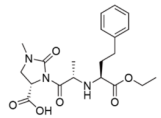
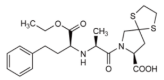
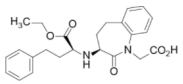
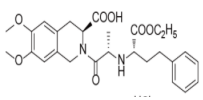
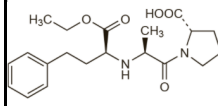
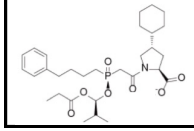
Anti-diabetic Agent (α-glucosidase Inhibitor)							
Structure	Formular	Name	Number	M.W.	MOA	Status	Indication
	$C_{25}H_{43}NO_{18}$	Acarbose	CAS No.56180-94-0 CID:41774 KEGG:D00216	645.608	α-glucosidase Inhibitor	Approved	T2DM
	$C_8H_{17}NO_5$	Miglitol	CAS No.72432-03-2 CID:441314 KEGG:D00625	207.2243	α-glucosidase Inhibitor	Approved	T2DM
	$C_6H_{13}NO_5$	Nojirimycin	CAS No.15218-38-9 CID:65242 KEGG:D06763	179.172	α-glucosidase Inhibitor	Unknown	Research
	$C_6H_{13}NO_4$	Duvoglustat	CAS No.19130-96-2 CID:29435 KEGG:C16843	163.173	α-glucosidase Inhibitor	Unknown	Research
	$C_{10}H_{21}NO_7$	Voglibose	CAS No.83480-29-9 CID:444020 KEGG:D01665	267.2762	α-glucosidase Inhibitor	Approved	T2DM
	$C_7H_{15}NO_5$	Alpha-Homonojirimycin	CID:159496	193.199	α-glucosidase Inhibitor	Unknown	Research

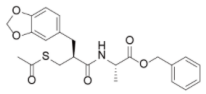
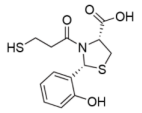
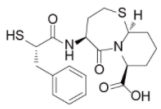
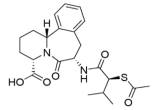
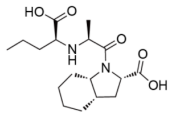
Total: 6

8.7 Angiotensin-Converting-Enzyme (ACE) Inhibitors

Antihypertensive Agent (ACE Inhibitor)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{22}H_{23}NO_4S_2$	Zofenopril	CAS No.81872-10-8 CID:92400 KEGG: D08688	429.552	ACE Inhibitor	Approved	Hypertension Myocardial infarction
	$C_{35}H_{42}N_2O_9$	Rescinnamine	CAS No.24815-24-5 CID:5280954 KEGG: D00198	634.716	ACE Inhibitor	Approved	Hypertension
	$C_{26}H_{32}N_2O_5$	Delapril	CAS No.83435-66-9 CID:5362116 KEGG: D07781	452.542	ACE Inhibitor	Approved	Hypertension
	$C_{23}H_{28}N_2O_5S_2$	Temoccapril	CAS No.111902-57-9 CID:71323 KEGG: D08566	476.608	ACE Inhibitor	Approved	Hypertension
	$C_{24}H_{34}N_2O_5$	Trandolapril	CAS No.87679-37-6 CID:5484727 KEGG: D00383	430.537	ACE Inhibitor	Approved	Hypertension
	$C_{22}H_{31}N_3O_5$	Cilazapril	CAS No.88768-40-5 CID:56330 KEGG: D07699	417.51	ACE Inhibitor	Approved	Hypertension Heart Failure
	$C_9H_{15}NO_3S$	Captopril	CAS NO.62571-86-2 CID:44093 KEGG: D00251	217.29	ACE Inhibitor	Approved	Hypertension Diabetic Nephropathy

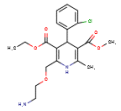
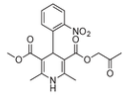
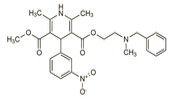
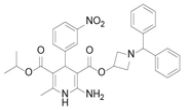
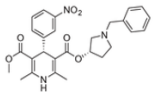
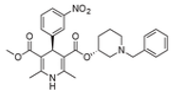
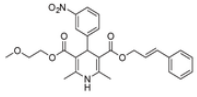
Antihypertensive Agent (ACE Inhibitor)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{25}H_{30}N_2O_5$	Quinapril	CAS No.85441-61-8 CID:54892 KEGG: D03752	438.516	ACE Inhibitor	Approved	Hypertension Heart Failure
	$C_{20}H_{26}N_2O_5S$	Alacepril	CAS No.74258-86-9 CID:71992 KEGG: D01900	406.49	ACE Inhibitor	Approved	Hypertension
	$C_{19}H_{32}N_2O_5$	Perindopril	CAS No.82834-16-0 CID:107807 KEGG: D03753	441.61	ACE Inhibitor	Approved	Hypertension Heart Failure Diabetic Nephropathy
	$C_{21}H_{31}N_3O_5$	Lisinopril	CAS No.83915-83-7 CID:5362119 KEGG: D00362	405.488	ACE Inhibitor	Approved	Hypertension Diabetic Nephropathy Heart Failure
	$C_{23}H_{32}N_2O_5$	Ramipril	CAS No.87333-19-5 CID:5362129 KEGG: D00421	416.511	ACE Inhibitor	Approved	Hypertension Diabetic Nephropathy Diabetic Renal
	$C_{19}H_{26}N_2O_4S$	Gemopatrilat	CAS No.160135-92-2 CID:9886079 KEGG: D04312	378.49	ACE Inhibitor	Phase II Discontinued	Hypertension Heart Failure
	$C_{26}H_{28}N_2O_5S$	MDL-100240	CAS No.14695-08-7 CID:133985	480.58	ACE Inhibitor	Phase II Discontinued	Hypertension Heart Failure
	$C_{26}H_{40}N_4O_9S$	Sampatrilat	CAS No.129981-36-8 CID:6324648	584.68	ACE Inhibitor & NEP Inhibitor	Phase II Discontinued	Hypertension Heart Failure

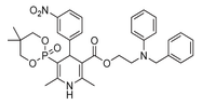
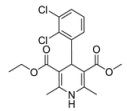
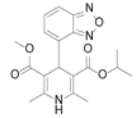
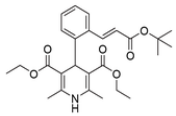
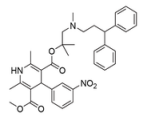
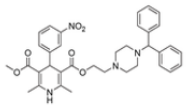
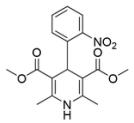
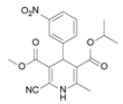
Antihypertensive Agent (ACE Inhibitor)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{11}H_{18}N_2O_5$	Idrapril	CAS No.127420-24-0 CID:65960	258.27	ACE Inhibitor	Phase II Discontinued	Hypertension
	$C_{22}H_{22}N_2O_3S_2$	Z-13752A	CAS No.193420-09-6 CID:9888720	426.55	ACE Inhibitor & NEP Inhibitor	Phase II Discontinued	Hypertension
	$C_{20}H_{27}N_3O_6$	Imidapril	CAS No.89371-37-9 CID:5464343 KEGG: D08068	405.44	ACE Inhibitor	Approved	Hypertension
	$C_{22}H_{30}N_2O_5S$	Spirapril	CAS No.83647-97-6 CID:5311447 KEGG: D08529	466.16	ACE Inhibitor	Approved	Hypertension
	$C_{24}H_{28}N_2O_5$	Benazepril	CAS No.86541-75-5 CID:5362124	424.49	ACE Inhibitor	Approved	Hypertension Heart Failure Renal-Failure
	$C_{27}H_{34}N_2O_7$	Moexipril	CAS No.103775-10-6 CID:91270 KEGG: D08225	498.568	ACE Inhibitor	Approved	Hypertension
	$C_{20}H_{28}N_2O_5$	Enalapril	CAS No.75847-73-3 CID:5388962 KEGG: D07892	376.447	ACE Inhibitor	Approved	Hypertension Heart Failure Kidney Disease
	$C_{30}H_{46}NO_7P$	Fosinopril	CAS No.98048-97-6 CID:55891 KEGG: D07992	563.663	ACE Inhibitor	Approved	Hypertension Heart Failure Diabetic-Nephropathy

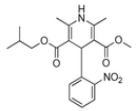
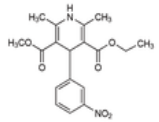
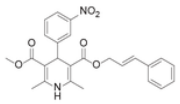
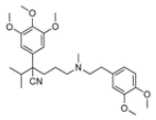
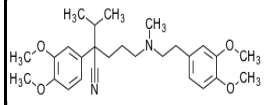
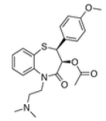
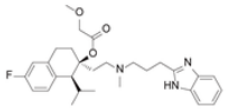
Antihypertensive Agent (ACE Inhibitor)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{23}H_{25}NO_6S$	Fasidotril	CAS No.135038-57-2 CID:5311337	443.51	ACE Inhibitor & NEP Inhibitor	Phase III Active	Hypertension Heart Failure
	$C_{13}H_{15}NO_4S_2$	Rentipril	CAS No.80830-42-8 CID:71244	313.39	ACE Inhibitor	Phase III Discontinued	Hypertension Heart Failure
	$C_{19}H_{24}N_2O_4S_2$	Omapatrilat	CAS No.167305-00-2 CID:656629 KEGG: D01970	408.534	ACE Inhibitor & NEP Inhibitor	Phase III Discontinued	Hypertension Heart Failure
	$C_{22}H_{28}N_2O_5S$	Ilepatril	CAS No.473289-62-2 CID:9824131	432.53	ACE Inhibitor & NEP Inhibitor	Phase II Discontinued	Hypertension Diabetic -Nephropathy
	$C_{17}H_{28}N_2O_5$	Perindoprilat	CAS No.95153-31-4 CID:72022	340.42	ACE Inhibitor	Phase I Discontinued	Hypertension Heart Failure

Total: 28

8.8 Calcium-Channel Blockers (CCBs)

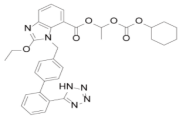
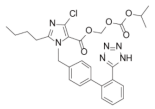
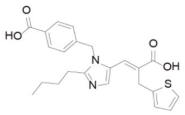
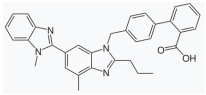
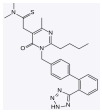
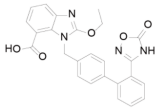
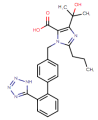
Antihypertensive Agent (Calcium Channel Blockers)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{20}H_{25}ClN_2O_5$	Amlodipine	CAS No.88150-42-9 CID:2162 KEGG: C06825	409.876	CCBs	Approved	Chronic Stable Angina Hypertension Vasospastic Angina
	$C_{19}H_{20}N_2O_7$	Aranidipine	CAS No.86780-90-7 CID:2225 KEGG: D015612	338.376	CCBs	Approved	Hypertension Angina Pectoris
	$C_{26}H_{29}N_3O_6$	Nicardipine	CAS No.55985-32-5 CID:4474 KEGG: C07264	479.525	CCBs	Approved	Chronic Stable Angina Hypertension
	$C_{33}H_{34}N_4O_6$	Azelnidipine	CAS No.123524-52-7 CID:65948 KEGG: D01145	582.657	CCBs	Approved	Hypertension
	$C_{27}H_{29}N_3O_6$	Barnidipine	CAS No.104713-75-9 CID:443869	491.544	CCBs	Approved	Chronic Stable Angina Hypertension
	$C_{28}H_{31}N_3O_6$	Benidipine	CAS No.105979-17-7 CID:656667	505.571	CCBs	Approved	Hypertension Angina Pectoris
	$C_{27}H_{28}N_2O_7$	Cilnidipine	CAS No.132203-70-4 CID:5282138 KEGG: D01173	492.528	CCBs	Approved	Hypertension

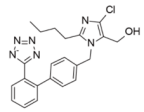
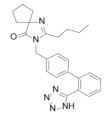
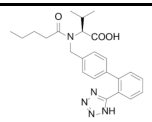
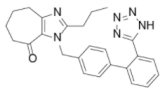
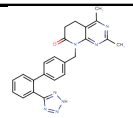
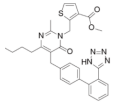
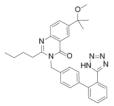
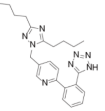
Antihypertensive Agent (Calcium Channel Blockers)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{34}H_{38}N_3O_7P$	Efonidipine	CAS No.111011-63-3 CID:119171	631.666	CCBs	Approved	Hypertension
	$C_{18}H_{19}Cl_2NO_4$	Felodipine	CAS No.72509-76-3 CID:3333 KEGG: D00319	384.254	CCBs	Approved	Hypertension Angina Pectoris
	$C_{19}H_{21}N_3O_5$	Isradipine	CAS No.75695-91-1 CID:3784 KEGG: D00349	371.3871	CCBs	Approved	Hypertension
	$C_{26}H_{33}NO_6$	Lacidipine	CAS No.103890-78-4 CID:5311217 KEGG: D04657	455.551	CCBs	Approved	Hypertension
	$C_{36}H_{41}N_3O_6$	Lercanidipine	CAS No.100427-26-7 CID:65866	611.7272	CCBs	Approved	Hypertension Angina Pectoris
	$C_{35}H_{38}N_4O_6$	Manidipine	CAS No.89226-50-6 CID:4008	610.711	CCBs	Approved	Hypertension
	$C_{17}H_{18}N_2O_6$	Nifedipine	CAS No.21829-25-4 CID:4485 KEGG: D00437	346.3346	CCBs	Approved	Hypertension Angina Pectoris
	$C_{19}H_{19}N_3O_6$	Nilvadipine	CAS No.75530-68-6 CID:4494 KEGG: D01908	385.3707	CCBs	Approved	Chronic Stable Angina Hypertension

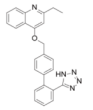
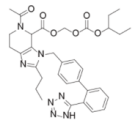
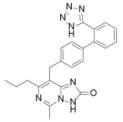
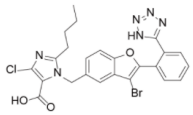
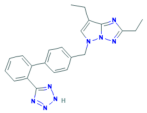
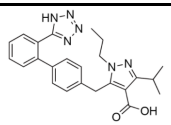
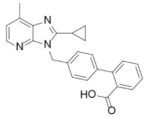
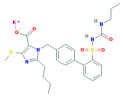
Antihypertensive Agent (Calcium Channel Blockers)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{20}H_{24}N_2O_6$	Nisoldipine	CAS No.63675-72-9 CID:4499 KEGG: D00618	388.4144	CCBs	Approved	Hypertension Angina Pectoris
	$C_{18}H_{20}N_2O_6$	Nitrendipine	CAS No.39562-70-4 CID:4507 KEGG: D00629	360.3612	CCBs	Approved	Hypertension
	$C_{25}H_{24}N_2O_6$	Pranidipine	CAS No.99522-79-9 CID: 6436048	448.475	CCBs	NDA Filing	Hypertension Angina Pectoris
	$C_{28}H_{40}N_2O_5$	Gallopamil	CAS No.16662-46-7 CID:1234 KEGG: D01969	484.637	CCBs	Approved	Hypertension Arrhythmia Angina Pectoris
	$C_{27}H_{38}N_2O_4$	Verapamil	CAS No.52-53-9 CID:2520 KEGG: D02356	454.6016	CCBs	Approved	Hypertension Angina Pectoris
	$C_{22}H_{26}N_2O_4S$	Diltiazem	CAS No.42399-41-7 CID:39186 KEGG: C06958	414.518	CCBs	Approved	Hypertension Angina Pectoris
	$C_{29}H_{38}FN_3O_3$	Mibefradil	CAS No.116644-53-2 CID:60663 KEGG: C07222	495.6287	CCBs	Withdrawn	Hypertension Angina Pectoris

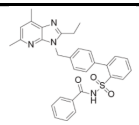
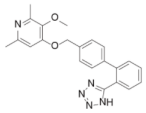
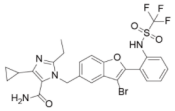
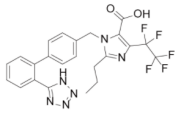
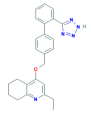
Total: 22

8.9 Angiotensin-Receptor Blockers (ARBs)

Antihypertensive Agent (ARBs)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{33}H_{34}N_6O_6$	Candesartan Cilexetil	CAS No.145040-37-5	610.67	ARBs	Approved	Hypertension Heart Failure
	$C_{27}H_{29}ClN_6O_5$	Allisartan Isoproxil	CAS No.947331-05-7	553.01	ARBs	Approved	Hypertension
	$C_{23}H_{24}N_2O_4S$	Eprosartan	CAS No.133040-01-4 CID:5281037 KEGG: D04040	520.625	ARBs	Approved	Hypertension
	$C_{33}H_{30}N_4O_2$	Telmisartan	CAS No.144701-48-4 CID:65999 KEGG: D00627	514.617	ARBs	Approved	Hypertension Diabetic Nephropathy
	$C_{27}H_{31}N_7OS$	Fimasartan	CAS No.247257-48-3 CID:9870652 KEGG: D10556	501.656	ARBs	Approved	Hypertension
	$C_{30}H_{24}N_4O_8$	Azilsartan	CAS No.147403-030-0	456.45	ARBs	Approved	Hypertension
	$C_{24}H_{26}N_6O_3$	Olmesartan	CAS No.144689-63-4	446.502	ARBs	Approved	Hypertension

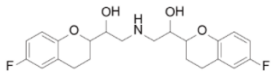
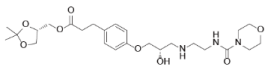
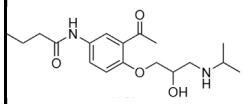
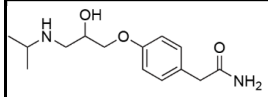
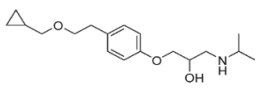
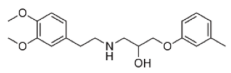
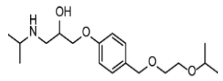
Antihypertensive Agent (ARBs)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{22}H_{23}ClN_6O$	Losartan	CAS No.114798-26-4	422.911	ARBs	Approved	Hypertension Diabetic Nephropathy
	$C_{25}H_{28}N_6O$	Irbesartan	CAS No.138402-11-6 CID:3749 KEGG: D00523	428.5294	ARBs	Approved	Hypertension Diabetic Nephropathy
	$C_{24}H_{29}N_5O_3$	Valsartan	CAS No.137862-53-4 CID:60846 KEGG: D00400	435.52	ARBs	Approved	Hypertension
	$C_{25}H_{26}N_6O$	Pratosartan	CAS No.153804-05-8	426.51	ARBs	Phase III Pending	Hypertension
	$C_{23}H_{21}N_7O$	Tasosartan	CAS No.145733-36-4 CID:60919	411.46	ARBs	Approved	Hypertension
	$C_{30}H_{30}N_6O_3S$	Milfasartan	CAS No.148564-47-0	554.66	ARBs	Phase II Discontinued	Hypertension
	$C_{30}H_{32}N_6O_2$	CL-329167	CAS No.143945-39-5	508.61	ARBs	Phase II Pending	Hypertension
	$C_{23}H_{28}N_8$	Forasartan	CAS No.145216-43-9 CID:132706 KEGG: D04243	416.522	ARBs	Phase II Pending	Hypertension

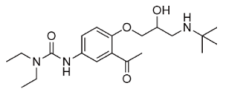
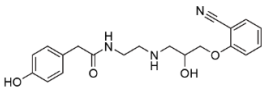
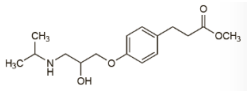
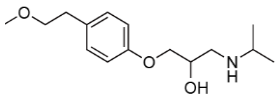
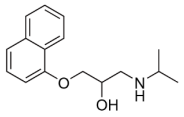
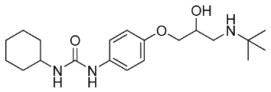
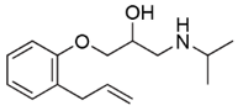
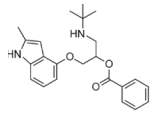
Antihypertensive Agent (ARBs)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{25}H_{21}N_5O$	ICI-D8731	CAS No.143494-72-8	407.475	ARBs	Phase II Discontinued	Hypertension Heart Failure
	$C_{33}H_{39}N_7O_6$	TA-606	CAS No.190602-72-3	629.716	ARBs	Phase I Pending	Hypertension
	$C_{23}H_{22}N_8O$	Ripisartan	CAS No.148504-51-2	426.47	ARBs	Phase II Discontinued	Hypertension
	$C_{24}H_{20}BrClN_6O_3$	Zolasartan	CAS No.145781-32-4	555.81	ARBs	Phase II Discontinued	Hypertension
	$C_{22}H_{22}N_8$	YM-358	CAS No.133052-30-9 CID:9801006	398.474	ARBs	Phase II Pending	Hypertension
	$C_{24}H_{26}N_6O_2$	UR-7247	CAS No.177847-28-8 CID:9802759	430.512	ARBs	Phase I Pending	Hypertension
	$C_{24}H_{21}N_3O_2$	E-4177	CAS No.135070-05-2 CID:131857	383.451	ARBs	Phase II Discontinued	Hypertension
	$C_{31}H_{30}N_4O_2$	Pomisartan	CAS No.144702-17-0 CID:3050407	490.607	ARBs	Phase II Pending	Hypertension

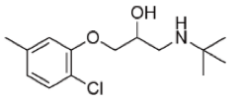
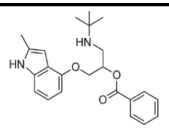
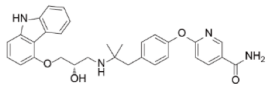
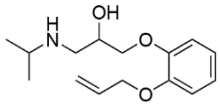
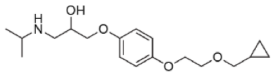
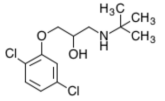
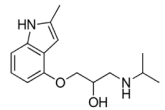
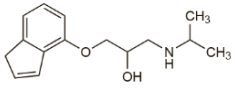
Antihypertensive Agent (ARBs)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{30}H_{28}N_4O_3S$	L-159282	CAS No.157263-00-8 CID:133031	524.639	ARBs	Phase II Pending	Hypertension
	$C_{22}H_{21}N_5O_2$	ME-3221	CAS No.139958-16-0 CID:178553	387.443	ARBs	Phase II Discontinued	Hypertension
	$C_{25}H_{22}BrF_3N_4O_4S$	Saprisartan	CAS No.146623-69-0 CID:60921	611.434	ARBs	Phase II Discontinued	Hypertension
	$C_{23}H_{19}F_5N_6O_2$	Dup-532	CAS No.124750-95-4 CID:60770	506.437	ARBs	Phase I Discontinued	Hypertension
	$C_{25}H_{25}N_5O$	ZD-6888	CAS No.138620-04-9 CID:9887844	411.509	ARBs	Phase I Discontinued	Hypertension

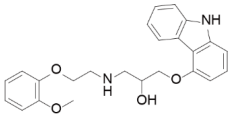
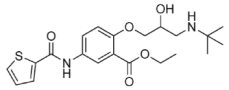
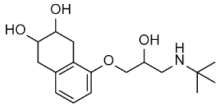
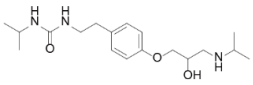
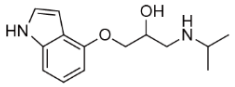
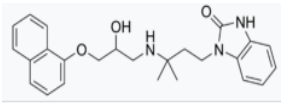
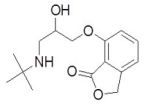
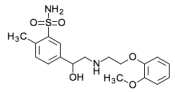
Total: 28

8.10 Adrenergic Antagonists

Antihypertensive Agent (Adrenergic Receptor Antagonists)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{22}H_{25}F_2NO_4$	Nebivolol	CAS No.118457-14-0 CID:71301 KEGG: D05127	405.435	ADRB1 Antagonist	Approved	Hypertension Diabetics Heart Failure
	$C_{25}H_{39}N_3O_8$	Landiolol	CAS No.133242-30-5 CID:164457 KEGG: D01847	509.6	β-AR Antagonist	Approved	Arrhythmia
	$C_{18}H_{28}N_2O_4$	Acebutolol	CAS No.37517-30-9 CID:1978 KEGG: D02338	336.4259	β-AR Antagonist	Approved	Hypertension Ventricular Dysfunction
	$C_{14}H_{22}N_2O_3$	Atenolol	CAS No.29122-68-7 PCID:2249 KEGG: D00235	266.3361	ADRB 1 Antagonist	Approved	Hypertension
	$C_{18}H_{29}NO_3$	Betaxolol	CAS No.63659-18-7 CID:2369 KEGG: D07526	307.4278	ADRB 1 Antagonist	Approved	Hypertension
	$C_{20}H_{27}NO_4$	Bevantolol	CAS No.59170-23-9 CID:2372 KEGG: D01369	345.4327	ADRB 1 Antagonist	Approved	Angina Pectoris Hypertension
	$C_{18}H_{31}NO_4$	Bisoprolol	CAS No.66722-44-9 CID:2405 KEGG: D02342	325.443	ADRB 1 Antagonist	Approved	Angina Pectoris Hypertension Heart Failure

Antihypertensive Agent (Adrenergic Receptor Antagonists)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{20}H_{33}N_3O_4$	Celiprolol	CAS No.56980-93-9 CID:2563 KEGG: D07660	379.501	ADRB 1 Antagonist	Approved	Angina Pectoris Hypertension
	$C_{20}H_{23}N_3O_4$	Epanolol	CAS No.86880-51-5 CID:72014 KEGG: D06646	369.421	ADRB 1 Antagonist	NDA Filling	Ischaemic Heart Disorder
	$C_{16}H_{25}NO_4$	Esmolol	CAS No.81147-92-4 CID:59768 KEGG: D07916	295.374	ADRB 1 Antagonist	Approved	Antiarrhythmia Hypertension
	$C_{15}H_{25}NO_3$	Metoprolol	CAS No.51384-51-1 CID:4171 KEGG: D02358	267.3639	β-AR Antagonist	Approved	Hypertension Heart Failure Angina Pectoris
	$C_{16}H_{21}NO_2$	Propranolol	CAS No.525-66-6 CID:4946 KEGG: C07407	259.3434	β-AR Antagonist	Approved	Hypertension Arrhythmia Angina Pectoris
	$C_{20}H_{33}N_3O_3$	Talinolol	CAS No.57460-41-0 CID:68770	363.4943	β-AR Antagonist	Approved	Hypertension
	$C_{15}H_{23}NO_2$	Alprenolol	CAS No.13655-52-2 CID:2119 KEGG: D07156	249.3486	β-AR Antagonist	Withdrawn	Hypertension
	$C_{23}H_{28}N_2O_3$	Bopindolol	CAS No.62658-63-4 CID:44112 KEGG: D07537	380.48	β-AR Antagonist	Approved	Hypertension Angina Pectoris

Antihypertensive Agent (Adrenergic Receptor Antagonists)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{14}H_{22}ClNO_2$	Bupranolol	CAS No.14556-46-8 CID:2475 KEGG: D07590	271.783	β-AR Antagonist	Approved	Hypertension Tachycardia
	$C_{16}H_{24}N_2O_3$	Carteolol	CAS No. 51781-06-7 CID:2583 KEGG: C06864	292.3734	β-AR Antagonist	Approved	Hypertension Angina Pectoris
	$C_{31}H_{32}N_4O_4$	LY-377604	CAS No.204592-94-9 CID:9849699	524.621	β-AR Antagonist	Phase II Discontinued	Obesity
	$C_{15}H_{23}NO_3$	Oxprenolol	CAS No.452-71-7 CID:4631 KEGG: D08318	265.348	β-AR Antagonist	Approved	Hypertension Arrhythmia Angina Pectroris
	$C_{18}H_{29}NO_4$	Cicloprolol	CAS No.94651-09-9 CID:146294	323.433	β-AR Antagonist	NDA Filling	Heart Failure Hypertension Ischaemic Heart Disorder
	$C_{13}H_{19}Cl_2NO_2$	Cloranolol	CAS No.39563-28-5 CID:65814 KEGG: D07183	292.2015	β-AR Antagonist	Unknow	Arrhythmia
	$C_{15}H_{22}N_2O_2$	Mepindolol	CAS No.23694-81-7 CID:71698 KEGG: D07181	262.353	β-AR Antagonist	Approved	Cardiovascular disorders
	$C_{15}H_{21}NO_2$	Indenolol	CAS No. 60607-68-3 CID:71955 KEGG: D08078	247.3327	β-AR Antagonist	Approved	Cardiovascular disorders

Antihypertensive Agent (Adrenergic Receptor Antagonists)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{24}H_{26}N_2O_4$	Carvedilol	CAS No.72956-09-3 CID:2585 KEGG: D 00255	406.4742	α/β-AR Antagonist	Approved	Hypertension Heart Failure Angina Pectoris
	$C_{21}H_{28}N_2O_5S$	Tienoxolol	CAS No.90055-97-3 CID:65678	420.524	β-AR Antagonist	Phase II Discontinued	Hypertension Ischaemic Heart Disorder
	$C_{17}H_{27}NO_4$	Nadolol	CAS No.42200-33-9 CID:39147 KEGG: D00432	309.4006	β-AR Antagonist	Approved	Hypertension Arrhythmia Angina Pectoris
	$C_{18}H_{31}N_3O_3$	Pafenolol	CAS No.80015-07-2 CID:71144	337.464	β-AR Antagonist	Phase I Discontinued	Antiarrhythmia
	$C_{14}H_{20}N_2O_2$	Pindolol	CAS No.13523-86-9 CID:4828 KEGG: D00513	248.3209	β-AR Antagonist	Approved	Hypertension Angina Pectoris
	$C_{25}H_{29}N_3O_3$	Adimolol	CAS No.78459-19-5 CID:71227	419.525	β-AR Antagonist	Research	Hypertension
	$C_{15}H_{21}NO_4$	Afurolol	CAS No.65776-67-2 CID:176877	279.336	β-AR Antagonist	Research	Hypertension
	$C_{18}H_{23}N_2O_5S$	Amosulaolo	CAS No.85320-68-9 CID:2169 KEGG: D07451	380.1406	β-AR Antagonist	Approved	Hypertension

Antihypertensive Agent (Adrenergic Receptor Antagonists)							
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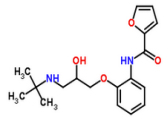
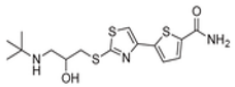
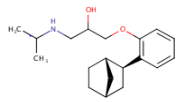
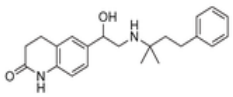
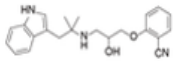
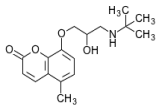
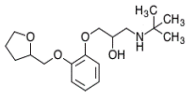
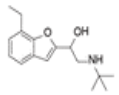
	$C_{1824}N_2O_4$	Ancarolol	CAS No.75748-50-4 CID:170339	332.4	β-AR Antagonist	Research	Hypertension
	$C_{15}H_{21}N_3O_2S_3$	Arotinolol	CAS No.68377-92-4 CID:2239 KEGG: D07465	371.53	β-AR Antagonist	Approved	Hypertension Arrhythmia Angina Pectoris
	$C_{19}H_{29}NO_2$	Bornaprolol	CAS No.66451-06-7 CID:68863	303.45	β-AR Antagonist	Unknown	Unknown
	$C_{22}H_{28}N_2O_2$	Brefonalol	CAS No.104051-20-9 CID:65880	352.487	β-AR Antagonist	Phase II Discontinued	Hypertension Arrhythmia Angina Pectoris
	$C_{22}H_{25}N_3O_2$	Bucindolol	CAS No.71119-11-4 CID:51045 KEGG: D031710	363.461	β-AR Antagonist	NDA Filling	Chronic Heart Failure Atrial Fibrillation
	$C_{17}H_{23}NO_4$	Bucumolol	CAS No.58409-59-9 CID:169787 KEGG: D01492	305.37	β-AR Antagonist	Unknown	Arrhythmia
	$C_{18}H_{29}NO_4$	Bufetolol	CAS No.53684-49-4 CID:2465 KEGG: D01504	323.43	β-AR Antagonist	Unknown	Arrhythmia
	$C_{16}H_{23}NO_2$	Bufuralol	CAS No.54340-62-4 CID:71733 KEGG: C13769	261.3593	β-AR Antagonist	Phase III Discontinued	Hypertension

Antihypertensive Agent (Adrenergic Receptor Antagonists)							
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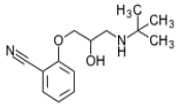
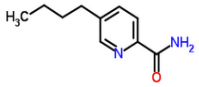
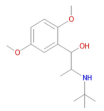
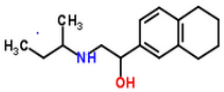
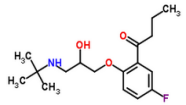
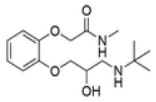
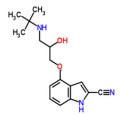
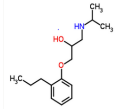
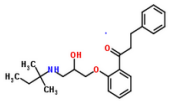
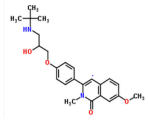
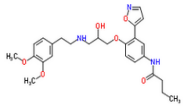
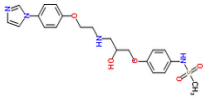
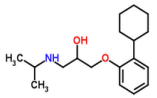
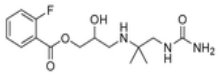
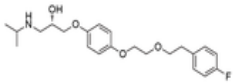
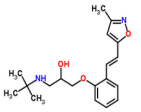
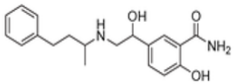
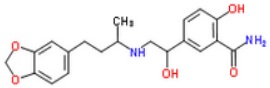
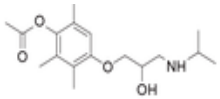
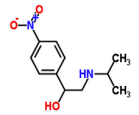
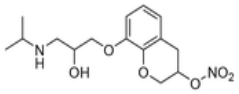
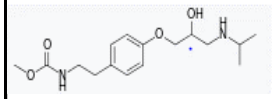
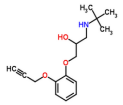
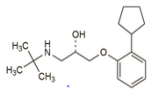
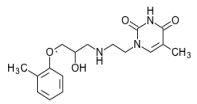
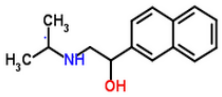
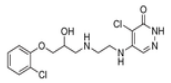
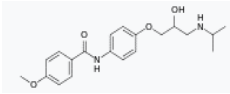
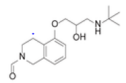
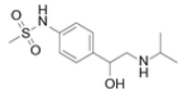
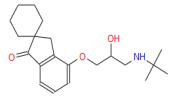
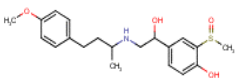
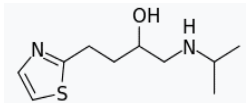
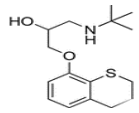
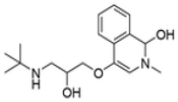
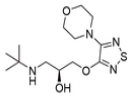
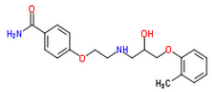
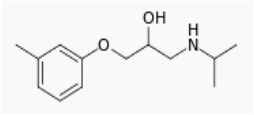
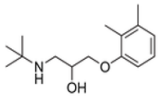
	$C_{14}H_{20}N_2O_2$	Bunitrolol	CAS No.34915-68-9 CID:2473 KEGG: D1444	248.326	α/β-AR Antagonist &	Unknown	Hypertension
	$C_{10}H_{14}N_2O$	Bupicomide	CAS No.22632-06-0 CID:31447	178.24	β-AR Antagonist	Research	Hypertension Vasodilator
	$C_{15}H_{25}NO_3$	Butaxamine	CAS No.2922-20-5 CID:21909	267.364	ADRB 2 Antagonist	Research	Hypolipidemia
	$C_{16}H_{25}NO$	Butidrine	CAS No.7433-10-5 CID:15177	247.382	β-AR Antagonist	Research	Arrhythmia
	$C_{17}H_{26}FNO_3$	Butofilolol	CAS No.64552-17-6 CID:68838	311.397	β-AR Antagonist	Research	Hypertension Arrhythmia Angina Pectoris
	$C_{16}H_{26}N_2O_4$	Cetamolol	CAS No.77590-95-5 CID:53698	310.394	ADRB 1 Antagonist	Phase III Discontinued	Hypertension
	$C_{16}H_{21}N_3O_2$	Cyanopindolol	CAS No.69906-85-0 CID:155346	287.363	β-AR Antagonist	Research	Hypertension Arrhythmia Angina Pectoris
	$C_{15}H_{25}NO_2$	Dihydroalprenolol	CAS No.60106-89-0 CID:43216	251.37	β-AR Antagonist	Research	Hypertension Arrhythmia Angina Pectoris

Antihypertensive Agent (Adrenergic Receptor Antagonists)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{23}H_{31}NO_3$	Diprafenone	CAS No.81447-80-5 CID:71249	369.51	β-AR Antagonist	Research	Arrhythmia
	$C_{24}H_{30}N_2O_4$	Draquinolol	CAS No.67793-71-9 CID:10070156	410.514	ADRB 1 Antagonist	Research	Heart Failure
	$C_{26}H_{33}N_3O_6$	Ecastolol	CID:208905	483.565	β-AR Antagonist	Phase I Discontinued	Hypertension
	$C_{21}H_{26}N_4O_5S$	Ersentilide	CAS No.125228-82-2 CID:130400	446.522	β-AR Antagonist	Research	Arrhythmia
	$C_{18}H_{29}NO_2$	Exaprolol	CAS No.55837-19-9 CID:65485	291.435	β-AR Antagonist	Research	Hypertension Arrhythmia Angina Pectoris
	$C_{15}H_{22}FN_3O_4$	Flestolol	CAS No.87721-62-8 CID:55885	327.356	β-AR Antagonist	Phase III Discontinued	Arrhythmia Ischaemic Heart Disorder
	$C_{22}H_{30}FNO_4$	Flusoxolol	CAS No.81228-25-5 CID:71765	391.483	β-AR Antagonist	Phase I Discontinued	Ischaemic Heart Disorder
	$C_{19}H_{26}N_2O_3$	Isoxaprolol	CAS No.75949-60-9 CID:6443854	330.428	β-AR Antagonist	Research	Hypertension Arrhythmia

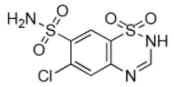
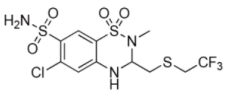
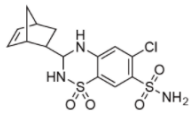
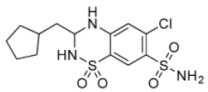
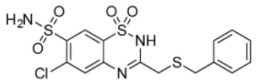
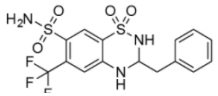
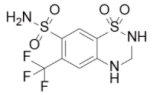
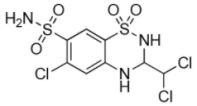
Antihypertensive Agent (Adrenergic Receptor Antagonists)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{19}H_{24}N_2O_3$	Labetalol	CAS No.36894-69-6 CID:3869 KEGG: D08106	328.4055	β-AR Antagonist	Approved	Hypertension
	$C_{20}H_{24}N_2O_5$	Medroxalol	CAS No.56290-94-9 CID:41835	372.421	α/β-AR Antagonist	Research	Hypertension Arrhythmia Angina Pectoris
	$C_{17}H_{27}NO_4$	Metipranolol	CAS No.22664-55-7 CID:31477 KEGG: D02374	309.4006	β-AR Antagonist	Approved	Hypertension Arrhythmia
	$C_{11}H_{16}N_2O_3$	Nifenalol	CAS No.7413-36-7 CID:6317	224.26	β-AR Antagonist	Research	Hypertension
	$C_{15}H_{22}N_2O_6$	Nipradilol	CAS No.81486-22-8 CID:72006	326.349	β-AR Antagonist	Research	Hypertension Arrhythmia Angina Pectoris
	$C_{16}H_{26}N_2O_4$	Pamatolol	CAS No.59110-35-9 CID:43150	310.394	β-AR Antagonist	Research	Hypertension
	$C_{16}H_{23}NO_3$	Pargolol	CID:68673	227.364	β-AR Antagonist	Research	Arrhythmia
	$C_{18}H_{29}NO_2$	Penbutolol	CAS No.38363-40-5 CID:37464 KEGG: D00602	291.4284	β-AR Antagonist	Approved	Hypertension Heart Disease

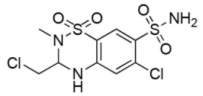
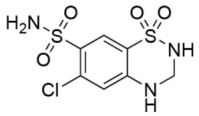
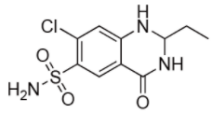
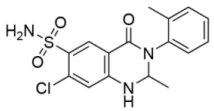
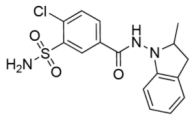
Antihypertensive Agent (Adrenergic Receptor Antagonists)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{17}H_{23}N_3O_4$	Primidolol	CAS No.67227-55-8 CID:68563 KEGG: C11774	333.1689	β-AR Antagonist	Research	Hypertension
	$C_{15}H_{19}NO$	Pronethalol	CAS No.54-80-8 CID:4930	229.323	β-AR Antagonist	Research	Heart Disease
	$C_{15}H_{18}Cl_2N_4O_3$	Ridazolol	CAS No.83395-21-5	373.234	ADRB1 Antagonist	Phase II Discontinued	Arrhythmia Ischaemic Heart Disorder
	$C_{20}H_{26}N_2O_4$	Ronactolol	CAS No.90895-85-5 CID:65824	358.438	β-AR Antagonist	Research	Heart Disease
	$C_{17}H_{26}N_2O_3$	Soquinolol	CAS No.61563-18-6 CID:68811	306.406	β-AR Antagonist	NDA Filling	Heart Failure
	$C_{12}H_{20}N_2O_3S$	Sotalol	CAS No.3930-20-9 CID:5253 KEGG: C07309	272.364	β-AR Antagonist	Approved	Arrhythmia
	$C_{21}H_{31}NO_3$	Spirendolol	CAS No.65429-87-0 CID:68857	345.483	β-AR Antagonist	Research	Hypertension
	$C_{20}H_{27}NO_4S$	Sulfinalol	CAS No.66264-77-5 CID: 44439	377.499	β-AR Antagonist	Research	Hypertension

Antihypertensive Agent (Adrenergic Receptor Antagonists)							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_9H_{16}N_2O_2S$	Tazolol	CAS No.39832-48-9 CID:71721	216.299	β-AR Antagonist	Research	Heart Disease
	$C_{16}H_{25}NO_2S$	Tertatolol	CAS No.34784-64-0 CID:36920 KEGG: D07182	295.4402	β-AR Antagonist	Approved	Hypertension Arrhythmia
	$C_{17}H_{24}N_2O_3$	Tilisolol	CAS No.85136-71-6 CID:5474 KEGG: D08598	304.3841	β-AR Antagonist	Approved	Hypertension Angina Pectoris
	$C_{13}H_{24}N_4O_3S$	Timolol	CAS No.26839-75-8 CID:33624 KEGG: D08600	316.42	β-AR Antagonist	Approved	Hypertension Heart Disease
	$C_{19}H_{24}N_2O_4$	Tolamolol	CID:37910	344.411	β-AR Antagonist	Research	Hypertension Angina Pectroris
	$C_{13}H_{21}NO_2$	Toliprolol	CID:18047	233.316	β-AR Antagonist	Research	Arrhythmia
	$C_{15}H_{25}NO_2$	Xibenolol	CAS No.30187-90-7 CID:146256	251.37	β-AR Antagonist	NDA Filling	Hypertension Ischaemic Heart Disorder

Total: 78

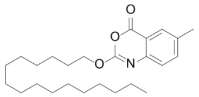
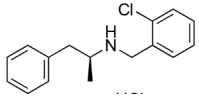
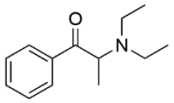
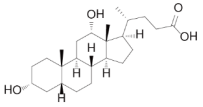
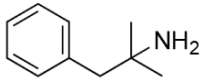
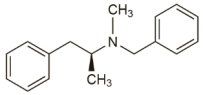
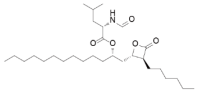
8.11 Thiazide Diuretics

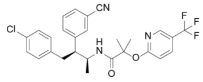
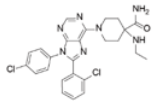
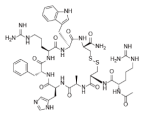
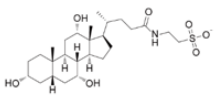
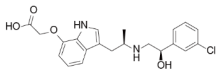
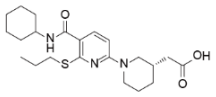
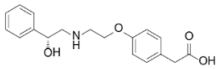
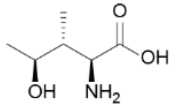
Antihypertensive Agent (Thiazide)							
Structure	Formular	Name	Number	M.W.	MOA	Status	Indication
	$C_7H_6ClN_3O_4S_2$	Chlorothiazide	CAS No.58-94-6 CID: 2720 KEGG: C07461	295.723	Thiazide	Approved	Hypertension-Diuretics
	$C_{11}H_{13}ClF_3N_3O_4S_3$	Polythiazide	CAS No.346-18-9 CID: 4870 KEGG: D00657	439.882	Thiazide	Approved	Hypertension Oedema
	$C_{14}H_{16}ClN_3O_4S_2$	Cyclothiazide	CAS No.2259-96-3 CID: 2910 KEGG: D01256	389.878	Thiazide	Approved	Hypertension Oedema
	$C_{13}H_{18}ClN_3O_4S_2$	Cyclopenthiazide	CAS No.742-20-1 CID: 2904 KEGG: D02061	379.88	Thiazide	Approved	Hypertension Oedema
	$C_{15}H_{14}ClN_3O_4S_3$	Benezhiazide	CAS No.91-33-8 CID: 2343 KEGG: D00651	431.937	Thiazide	Approved	Hypertension Oedema
	$C_{15}H_{14}F_3N_3O_4S_2$	Bendroflumethiazide	CAS No. 73-48-3 CID: 2315 KEGG: D00650	421.415	Thiazide	Approved	Hypertension Oedema
	$C_8H_8F_3N_3O_4S_2$	Hydroflumethiazide	CAS No. 135-09-1 CID: 3647 KEGG: D00654	331.292	Thiazide	Approved	Hypertension Heart failure
	$C_8H_8Cl_3N_3O_4S_2$	Trichlormethiazide	CAS No. 133-67-5 CID: 5560 KEGG: D00658	380.656	Thiazide	Approved	Hypertension Oedema

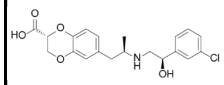
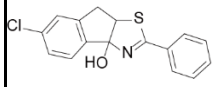
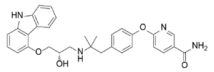
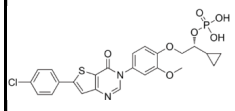
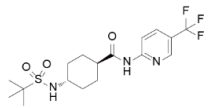
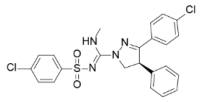
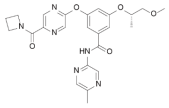
Antihypertensive Agent (Thiazide)							
Structure	Formular	Name	Number	M.W.	MOA	Status	Indication
	$C_9H_{11}Cl_2N_3O_4S_2$	Methyclothiazide	CAS No. 135-07-9 CID: 4121 KEGG: D00656	360.237	Thiazide	Approved	Hypertension
	$C_7H_8ClN_3O_4S_2$	Hydrochlorothiazide	CAS No. 58-93-5 CID: 3639 KEGG: D00340	297.739	Thiazide	Approved	Hypertension Oednma Diabetes Insipidus
	$C_{10}H_{12}ClN_3O_3S$	Quinethazone	CAS No. 73-49-4 CID: 6307 KEGG: D00461	289.739	Thiazide	Approved	Hypertension
	$C_{16}H_{16}ClN_3O_3S$	Metolazone	CAS No. 17560-51-9 CID: 4170 KEGG: D00431	365.835	Thiazide-like Diuretic	Approved	Hypertension Oedema Heart failure
	$C_{16}H_{16}ClN_3O_3S$	Indapamide	CAS No. 26807-65-8 CID: 3702 KEGG: D00345	365.835	Thiazide-like Diuretic	Approved	Hypertension

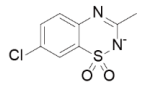
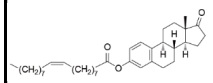
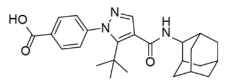
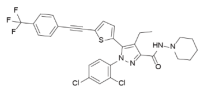
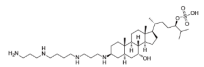
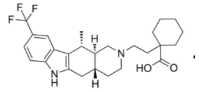
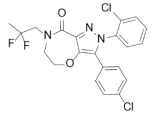
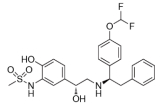
Total: 13

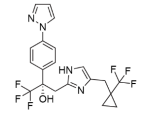
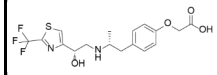
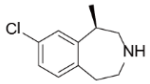
8.12 Anti-Obesity Agents

Anti-obesity Agents							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{25}H_{39}NO_3$	Cetilistat	CAS No.282526-98-1 CID:9952916	401.582	Lipase Inhibitor	Approved	Obesity
	$C_{16}H_{18}ClN$	Clobenzorex	CAS No.13364-32-4 CID:259777	259.777	CNS Stimulant	Withdrawn	Obesity
	$C_{13}H_{19}NO$	Diethylpropion	CAS No.90-84-6 CID:7029 KEGG: C06954	205.296	CNS Stimulant	Approved	Obesity
	$C_{24}H_{40}O_4$	Deoxycholic Acid	CAS No.83-44-3 CID:222528 KEGG: C04483	392.572	GPBAR1 Agonist	Approved	Localized Submental Fat
	$C_{10}H_{15}N$	Phentermine	CAS No.122-09-8 CID:4771 KEGG: D05458	149.233	β-Adrenergic Receptor Agonist	Approved	Obesity
	$C_{17}H_{21}N$	Benzfetamine	CAS No.156-08-1 CID:5311017 KEGG: C07538	239.355	Adrenergic Receptor Agonist	Approved	Obesity
	$C_{29}H_{53}NO_5$	Orlistat	CAS No.96829-58-2 CID:3034010	495.735	Gastrointestinal Lipase Inhibitor	Approved	Obesity

Anti-obesity Agents							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{27}H_{25}ClF_3N_3O_2$	Taranabant	CAS No.701977-09-5 CID:11226090	515.960	CB1 Inverse Agonists	Phase III Discontinued	Obesity
	$C_{25}H_{25}Cl_2N_7O$	Otenabant	CAS No.686344-29-6 CID:10052040	510.420	CB1 Inverse Agonist	Phase III Discontinued	Obesity
	$C_{49}H_{68}N_{18}O_9S_2$	Setmelanotide	CAS No.920014-72-8	1117.320	MC4-R Agonst	Phase III Active	Obesity
	$C_{26}H_{45}NO_7S$	Taurocholic Acid	CAS No.81-24-3 CID:6675 KEGG: C05122	515.703	GPBAR1 Agonists	Phase II Active	T2DM & Obesity
	$C_{21}H_{23}ClN_2O_4$	Rafabegron	CAS No.244081-42-3 CID:5493324	402.875	β3 Adrenergic Receptor Agonist	Phase II Discontinued	Diabetes & Obesity
	$C_{22}H_{33}N_3O_3S$	AZD-4017	CAS No.1024003-43-9 CID:24946280	419.584	11β-HSD 1 Inhibitor	Phase II Discontinued	T2DM & Obesity
	$C_{18}H_{21}NO_4$	Talibergon	CAS No.146376-58-1 CID 158794	315.369	β3 Adrenergic Receptor Agonist	Phase II Discontinued	T2DM & Obesity
	$C_6H_{13}NO_3$	ID-1101	CAS No.55399-93-4 CID:6918732	147.174	Insulin Sensitizer	Phase II Discontinued	T2DM & Obesity

Anti-obesity Agents							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{20}H_{22}ClNO_5$	N-5984	CAS No.220475-76-3 CID:9865284	391.848	β3 Adrenergic Receptor Agonist	Phase II Discontinued	T2DM & Obesity
	$C_{16}H_{12}ClNOS$	HMR-1426	CAS No.262376-75-0 CID:9882837	301.788	Gastric Emptying Inhibitor	Phase II Discontinued	T2DM & Obesity
	$C_{31}H_{32}N_4O_4$	LY-377604	CAS No.204592-97-2 CID:9849699	524.621	β-Adrenoceptor Agonist	Phase II Discontinued	Obesity
	$C_{24}H_{22}ClN_2O_7PS$	BMS-830216	CAS No.1197420-06-6 CID:4539266	548.931	MCH1R Inhibitor	Phase II Discontinued	Obesity
	$C_{17}H_{24}F_3O_3S$	Velneperit	CAS No.342577-38-2 CID:20629114	407.450	Neuropeptide Y5 Antagonists	Phase II Discontinued	Obesity
	$C_{24}H_{29}NO_6$	BRL-26830	CAS No.77955-41-0 CID: 6438331	427.497	β3 Adrenergic Receptor Agonist	Phase II Discontinued	Diabetes Hyperlipidemia Obesity
	$C_{23}H_{20}Cl_2N_4O_2S$	Ibipinabant	CAS No.464213-10-3 CID:9826744	487.400	Cannabinoid CB1 Antagonist	Phase II Discontinued	T2DM & Obesity
	$C_{24}H_{26}N_6O_5$	AZD-1656	CAS No.919783-22-5 CID:16039797	478.509	Glucokinase Activators	Phase II Discontinued	T2DM & Obesity

Anti-obesity Agents							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_8H_7ClN_2O_2S$	Diazoxide	CAS No.364-98-7 CID:3019 KEGG: D00294	230.666	Potassium channel agonists	Phase II Pending	Obesity & Hpertriglyceridemia
	$C_{36}H_{54}O_3$	Oleoyl-estrone	CAS No.180003-17-2 CID:6918373	534.812	Estrogen Receptor Agonist	Phase II Discontinued	Obesity
	$C_{25}H_{31}N_3O_3$	AZD-8329	CAS No.1048668-70-7 CID:25006684	421.541	CYP11B1 Inhibitors	Phase I Discontinued	T2DM & Obesity
	$C_{30}H_{25}Cl_2F_3N_4OS$	TM-38837	CAS No.1253641-65-4 CID:49779607	617.512	CB1 Antagonist	Phase I Pending	T2DM & Obesity
	$C_{37}H_{72}N_4O_5S$	Trodusquemine	CAS No.186139-09-3 CID:9917968	685.066	Protein Tyrosine Phosphatase Inhibitors	Phase I Discontinued	T2DM & Obesity
	$C_{26}H_{33}F_3N_2O_2$	AMG-076	CAS No.693823-79-9	462.557	SLC-1 Receptor Antagonist	Phase I Discontinued	Obesity
	$C_{21}H_{17}Cl_2F_2N_3O_2$	PF-514273	CAS No.851728-60-4	452.283	CB1 Antagonist	Phase I Discontinued	Obesity
	$C_{24}H_{26}F_2N_2O_5S$	BMS-196085	CAS No.170686-10-9	492.538	β3 Adrenergic Receptor Agonist	Phase I Discontinued	T2DM & Obesity

Anti-obesity Agents							
Structure	Formula	Name	Number	M.W.	MOA	Status	Indication
	$C_{20}H_{18}F_6N_4O$	MK-5046	CAS No.1022152-70-0 CID:49871766	444.381	Bombesin Receptor Subtype-3 Agonist	Phase I Pending	Obesity
	$C_{17}H_{19}F_3N_2O_4S$	CP-114272	CAS No.162326-86-5 CID:18551400	404.404	β3 Adrenergic Receptor Agonist	Phase I Pending	Obesity
	$C_{11}H_{14}ClN$	Lorcaserin	CAS No.616202-92-7 CID:11658860 KEGG: D06613	195.690	Selective 5-HT2C Receptor Agonist	Approved	Obesity

Total: 34

9. Table

Catalog	Classification	Total Numbers of Agents	Positive Results
Anti-diabetic Agents	6	92	5
Anti-hypertensive Agents	5	170	3
Anti-obesity Agents	--	34	--

Table 1. The summary of in-house Drug Library.

Anti-diabetic Agents	Description	Drugs	Results		
			11L	12M	13N
Dipeptidyl-peptidase-4 (DPP-4) Inhibitors	DPP-4 inhibitors are a class of oral anti-diabetic agents that block dipeptidyl peptidase-4 (DPP-4). They can be used to the management of T2DM.	34	1 (+) C15H18N6O	(-)	(-)
Sodium/Glucose co-transporter 2 (SGLT-2) Inhibitors	SGLT-2 Inhibitors block reabsorption of glucose in kidney to reduce glucose level in blood.	16	(-)	(-)	(-)
Sulfonylureas	Sulfonylureas facilitate insulin release and increase insulin sensitive of beta cells in the pancreas	16	1 (+) C15H20N2O4S	1 (+) C15H20N2O4S	(-)
Adenosine 5'-monophosphate Active Protein kinase (AMPK) Activators	AMPK is a central regulator of energy homeostasis, which increase glucose uptake, reduce cholesterol synthesis, and facilitate fatty acid catabolism by various metabolic pathways	9	(-)	2(+) C20H12N2O3 S C9H14N4O5	(-)
Peroxisome Proliferator-Activated Receptors (PPARs) Agonist	They used for the treatment of the metabolic syndrome to regulate glucose homeostasis and increase fatty acid oxidation.	11	(-)	(-)	(-)
Alpha Glucosidase Inhibitors	Alpha-glucosidase inhibitors are oral anti-diabetic drugs used for T2DM that work by preventing the digestion of carbohydrates.	6	1(+) C10H21NO7	1(+) C10H21NO7	(-)

Table 2. The summary of identified anti-diabetic agents (compounds)/(+)- in plants extraction.

Anti-hypertensive Agents	Description	Drugs	Results		
			11L	12M	13N
Angiotensin-Converting- Enzyme (ACE) Inhibitors	Angiotensin-converting-enzyme inhibitor (ACE inhibitor) is primarily for the treatment of hypertension and heart failure. And it is also useful to kidney diseases including kidney complication of diabetes mellitus.	28	(-)	(-)	(-)
Angiotensin-Receptor Blockers (ARBs)	Angiotensin II receptor blockers (ARBs) are a group of pharmaceuticals to treatment of hypertension, diabetic nephropathy (kidney damage due to diabetes) and congestive heart failure.	29	(-)	(-)	1 (+) C25H25N5O
Adrenergic Blockers	β-Blocker are class of medications that are particularly used to manage abnormal heart rhythms and heart attack. β - Blocker can reduce the risk of cardiovascular events and death in post myocardial infarction patients with diabetes.	78	(-)	2(+) C15H22N2O6 C16H24N2O3	(-)
Thiazide Diuretics	Thiazide diuretics are the class of medications to treat hypertension and congestive heart failure as well as the accumulation of fluid and swelling of the body caused by heart failure, chronic kidney failure and nephrotic syndrome.	13	(-)	(-)	(-)
Calcium-Channel Blockers (CCBs)	CCB is a class of drug to disrupt the movement of calcium through calcium cannels. It is commonly used as anti- hypertensive drugs.	22	(-)	(-)	(-)

Table 3. The summary of identified anti-hypertensive agents (compounds)/(+)- in plants extraction.

10. Figures

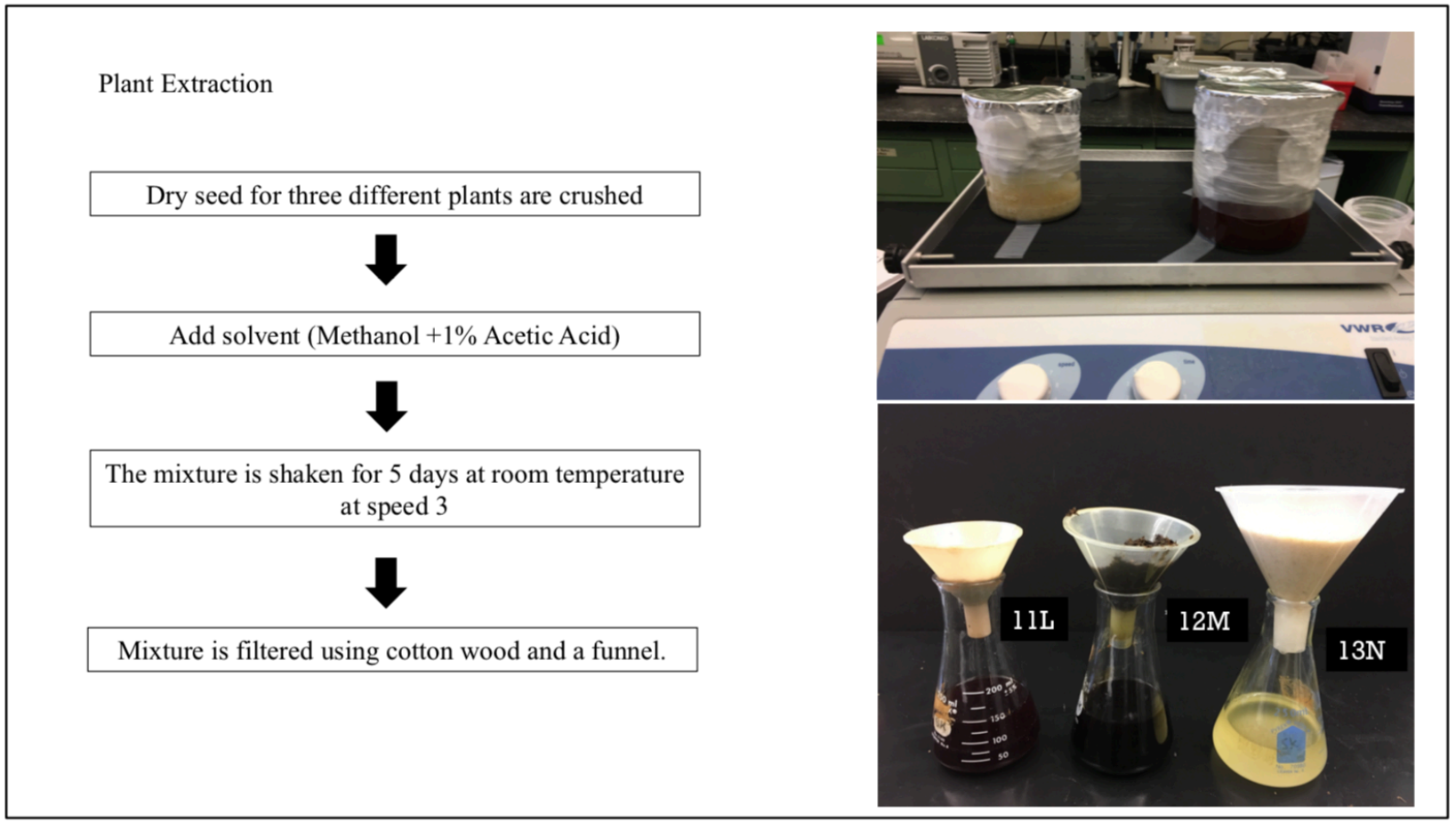


Figure 1. The method of compound extraction.

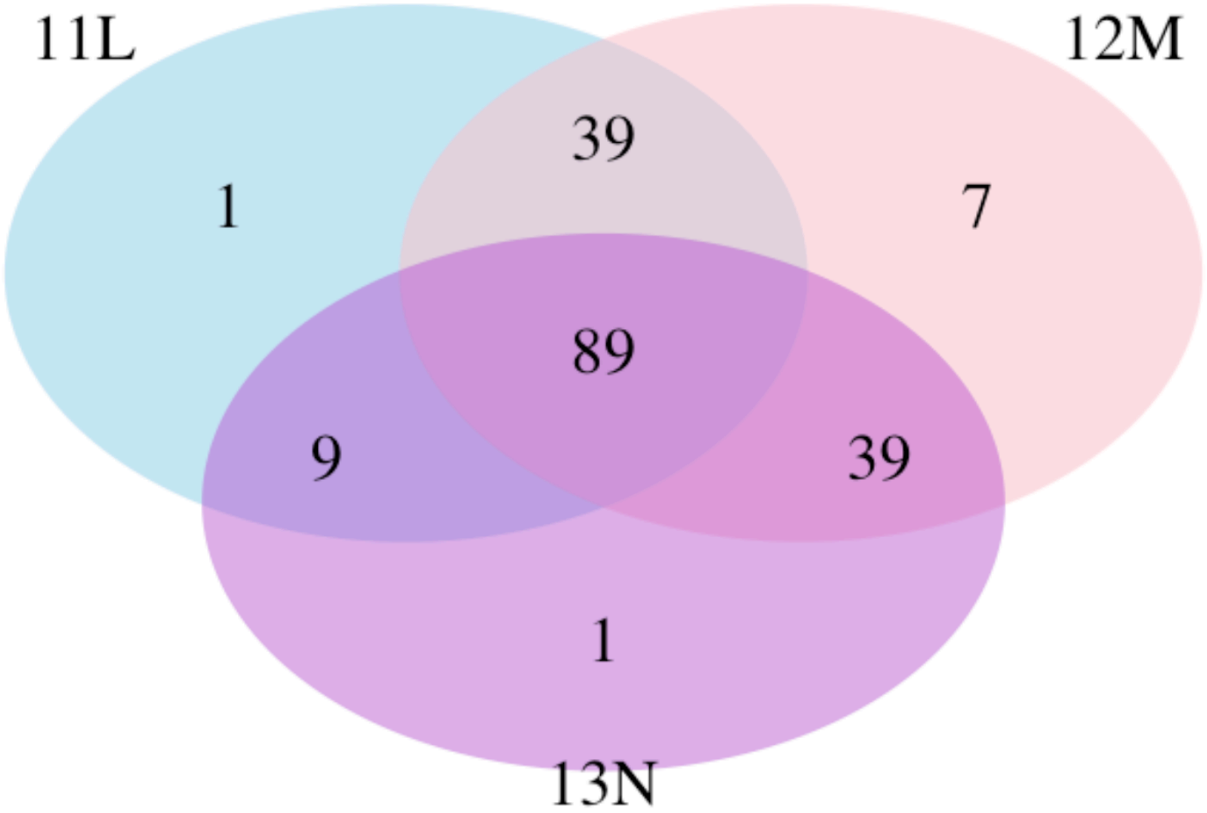


Figure 2. A venn diagram of identified compound of extraction of *Khaya Senegalensis* (11L), *Anacardium Occidentale* (12M), and *Moringa Oleifiera* (13M)

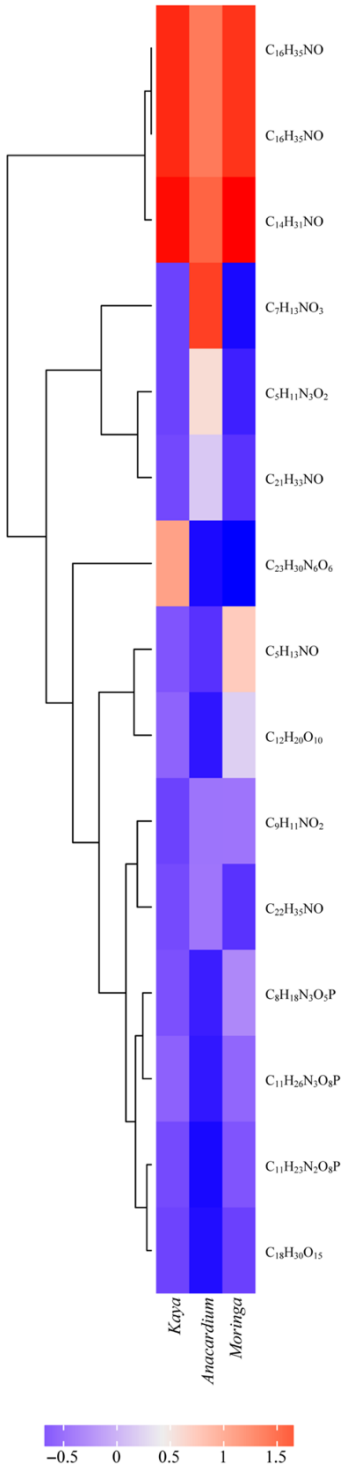


Figure 3. Heat map for identified compound (cluster 1-High-Intensity)

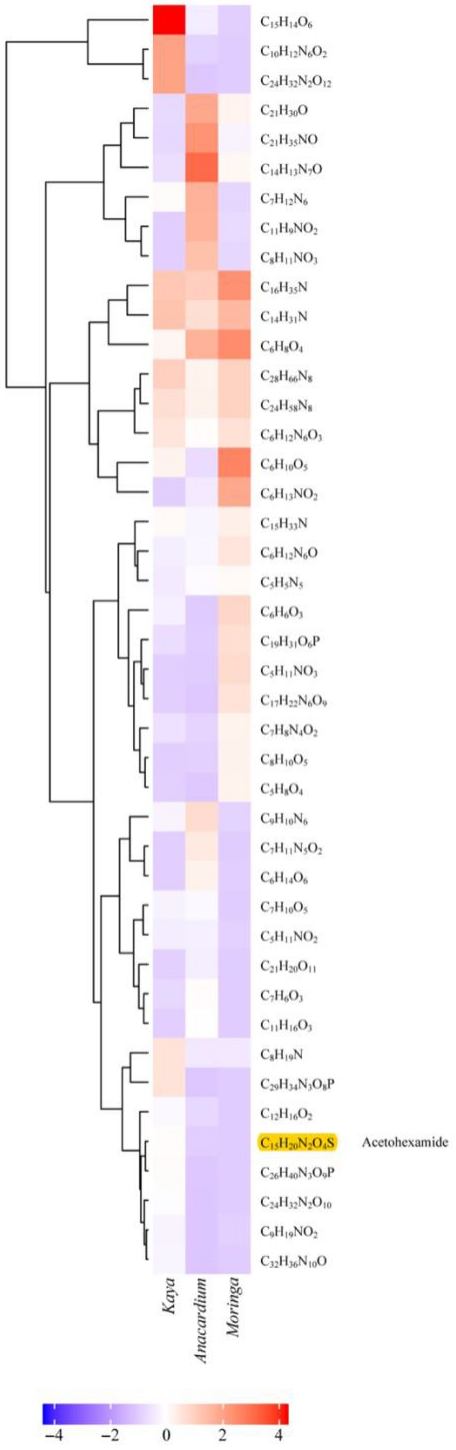


Figure 4. Heat map for identified compound cluster 2 (Identified drug is highlighted)

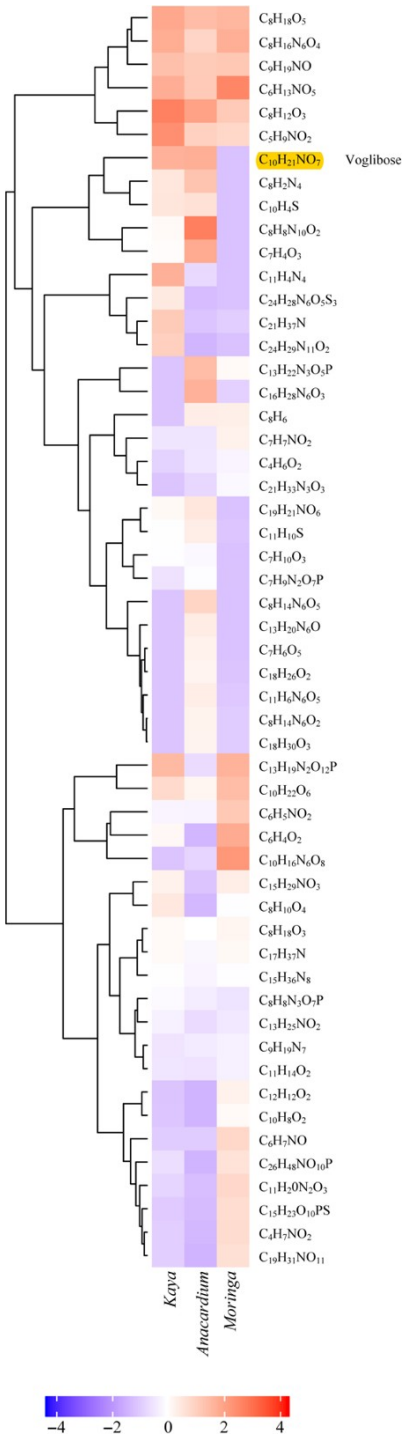


Figure 5. Heat map for identified compound cluster 3 (Identified drug is highlighted)

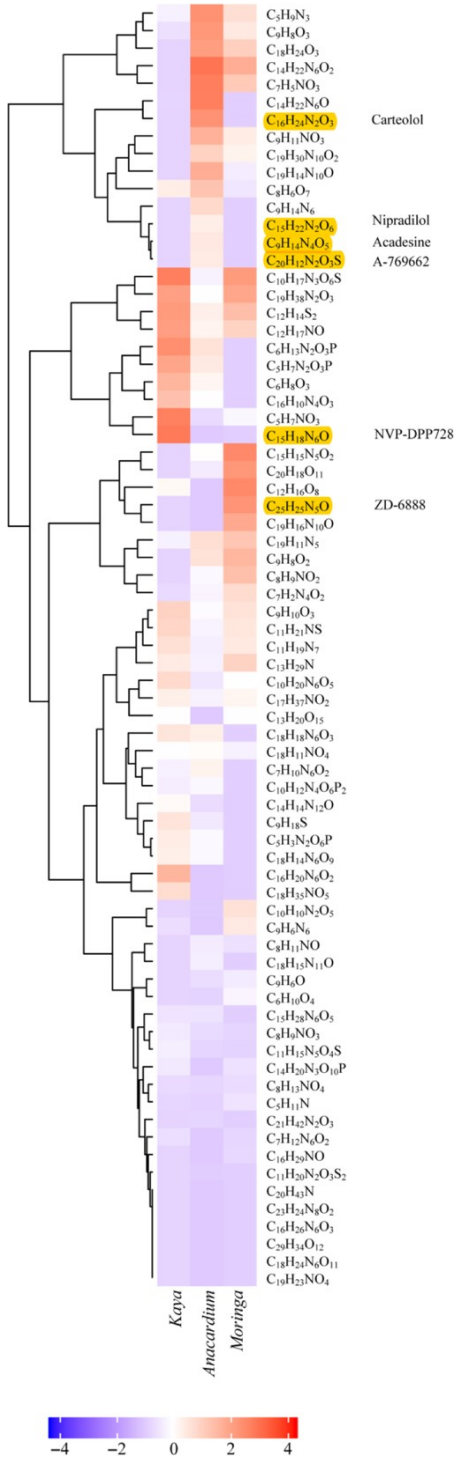
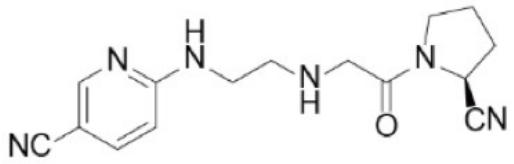


Figure 6. Heat map for identified compound cluster (Low intensity)
(Identified drug is highlighted)

NVP-DPP728 is a dipeptidyl peptidase-4 (DPP-4) inhibitor for the T2DM treatment developed by Novartis.



Chemical Structure

Formula:	$C_{15}H_{18}N_6O$
CAS No.:	247016-69-9
PubChem CID:	9796290
Retention Time:	18.2 min
Molar Mass:	298.34
Measured m/z [M+H]:	299.1615
Chemical Name:	6-[[2-[[2-(2S)-2-Cyano-1-pyrrolidinyl]-2-oxoethyl]amino]ethyl]amino-3-pyridinecarbononitrile

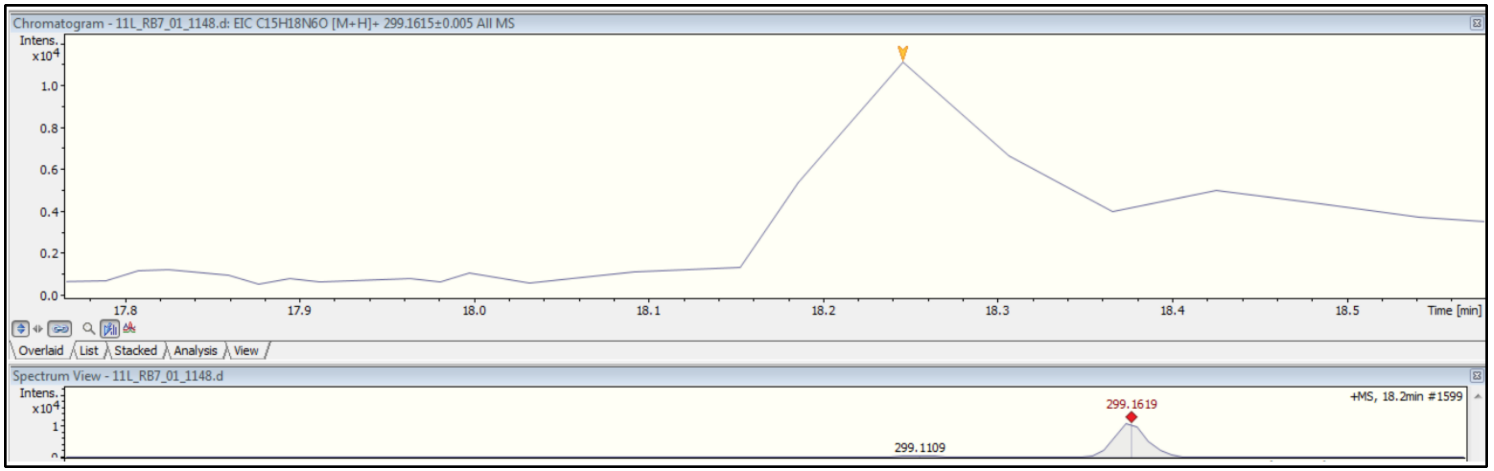
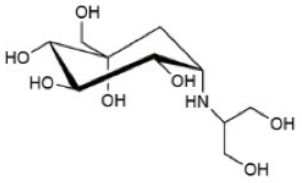


Figure 7. A DPP-4 Inhibitor (NVP-DPP728) found in *Khaya Senegalensis*.

Voglibose is an α-glucosidase inhibitor used for lowering post-prandial blood glucose levels in people with diabetes mellitus by preventing the digestion of complex carbohydrates. Voglibose was approved in Japan in 1994.



Chemical Structure

Formula:	$C_{10}H_{21}NO_7$
CAS No.:	83480-29-9
PubChem CID:	444020
Retention Time	7min
Molar Mass:	267.2762
Measured m/z [M+H]:	268.1391
Chemical Name:	1S,2S,3R,4S,5S)-5-(1,3-dihydroxypropan-2-ylamino)-1-(hydroxymethyl) cyclohexane -1,2,3,4-tetrol

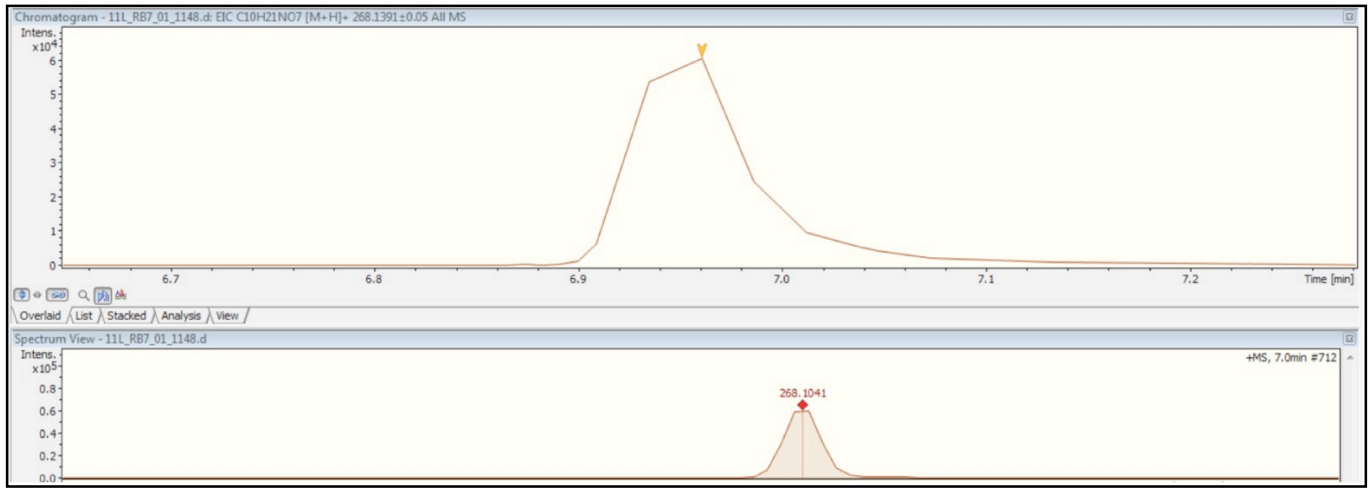
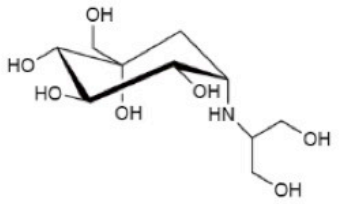


Figure 8. A α-glucosidase inhibitor (Voglibose) found in *Khaya Senegalensis* (11L).

Voglibose is an α-glucosidase inhibitor used for lowering post-prandial blood glucose levels in people with diabetes mellitus by preventing the digestion of complex carbohydrates. Voglibose was approved in Japan in 1994



Chemical Structure

Formula:	$C_{10}H_{21}NO_7$
CAS No.:	83480-29-9
PubChem CID:	444020
Retention Time	7min
Molar Mass:	267.2762
Measured m/z [M+H]:	268.1391
Chemical Name:	1S,2S,3R,4S,5S)-5-(1,3-dihydroxypropan-2-ylamino)-1-(hydroxymethyl) cyclohexane -1,2,3,4-tetrol

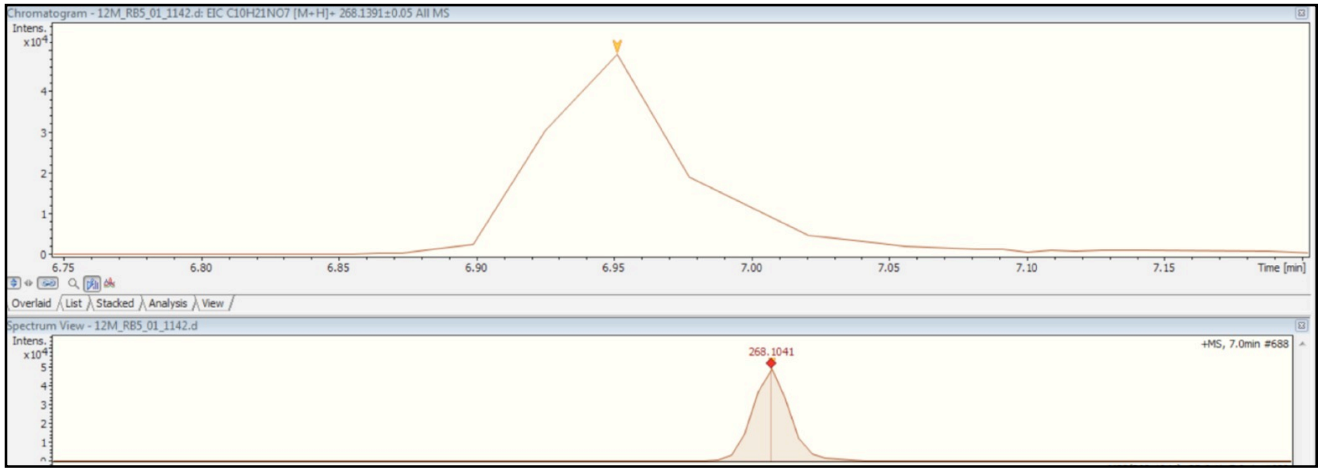
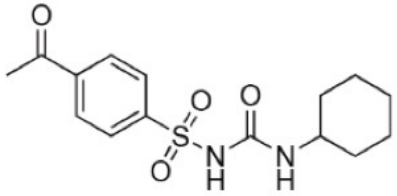


Figure 9. A α-glucosidase inhibitor (Voglibose) found in *Anacardium Occidentale* (12M).

Acetohexamide is the first-generation oral sulfonylurea for T2DM management, which stimulates β-cells to secrete more insulin and increase insulin sensitivity. However, Acetohexamide has been discontinued in the US market.



Chemical Structure

Formula: $C_{15}H_{20}N_2O_4S$
CAS No.: 968-81-0
PubChem CID: 1989
Retention Time: 2.7 min
Molar Mass: 324.395
Measured m/z [M+H]: 325.1217
Chemical Name: 1-((p-Acetylphenyl)sulfonyl)-3-cyclohexylurea

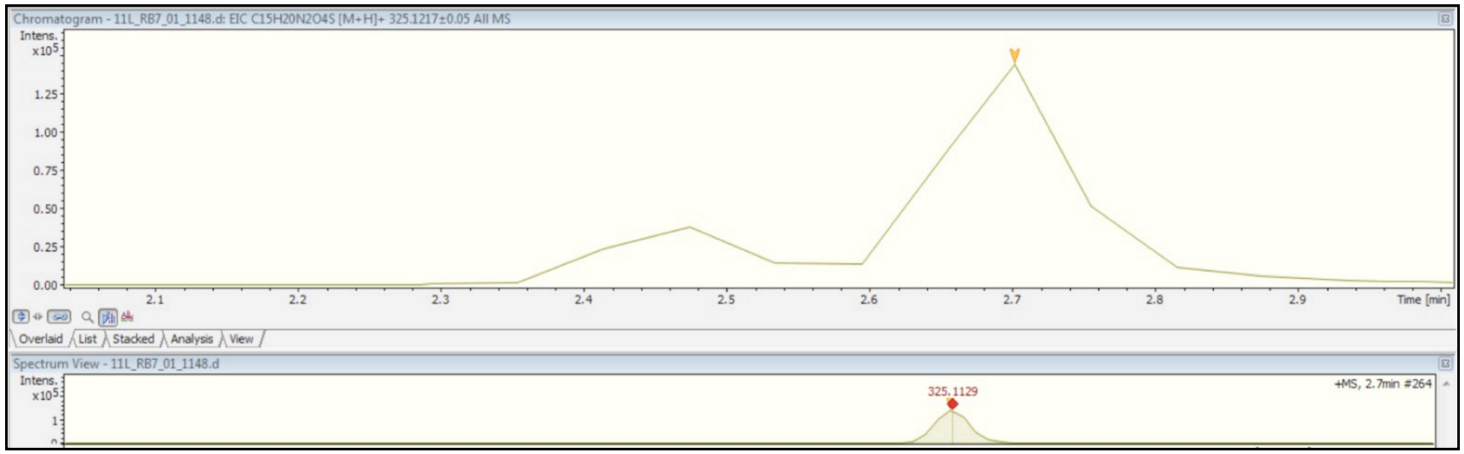
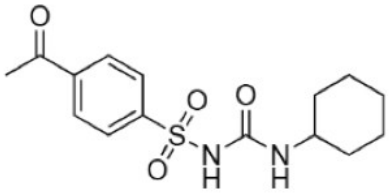


Figure 10. A first-generation sulfonylurea (Acetohexamide) found in *Khaya Senegalensis* (11L).

Acetohexamide is the first-generation oral sulfonylurea for T2DM management, which stimulates β-cells to secrete more insulin and increase insulin sensitivity. However, Acetohexamide has been discontinued in US market.



Chemical Structure

Formula: $C_{15}H_{20}N_2O_4S$
CAS No.: 968-81-0
PubChem CID: 1989
Retention Time: 2.5 min
Molar Mass: 324.395
Measured m/z [M+H]: 325.1217
Chemical Name: 1-((p-Acetylphenyl)sulfonyl)-3-cyclohexylurea

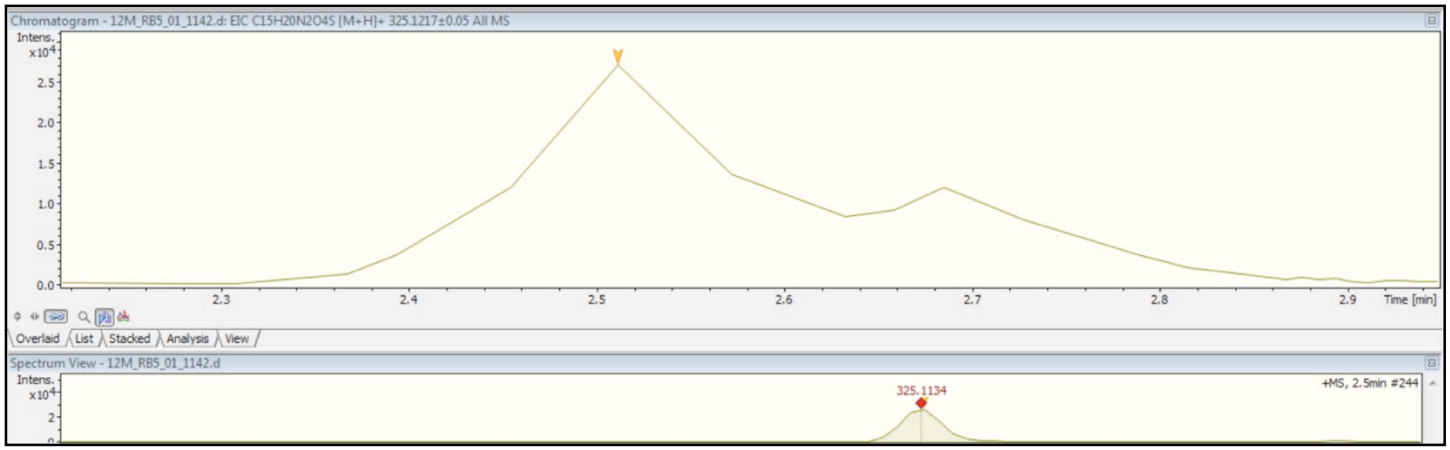
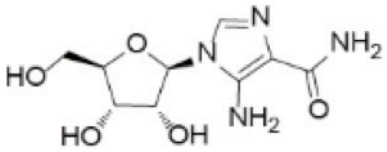


Figure 11. A first-generation sulfonylurea (Acetohexamide) found in *Anacardium Occidentale* (12M).

Acadesine is an AMPK activator for the treatment of impaired glucose tolerance, insulin resistance in both T1DM and T2DM with poor oral bioavailability, which limited its application.



Chemical Structure

Formula: $C_9H_{14}N_4O_5$
CAS No.: 844499-71-4
PubChem CID: 2627-69-2
Retention Time: 8.3 min
Molar Mass: 258.234
Measured m/z [M+H]: 259.1037
Chemical Name: 5-amino-1-[(2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]imidazole-4-carboxamide

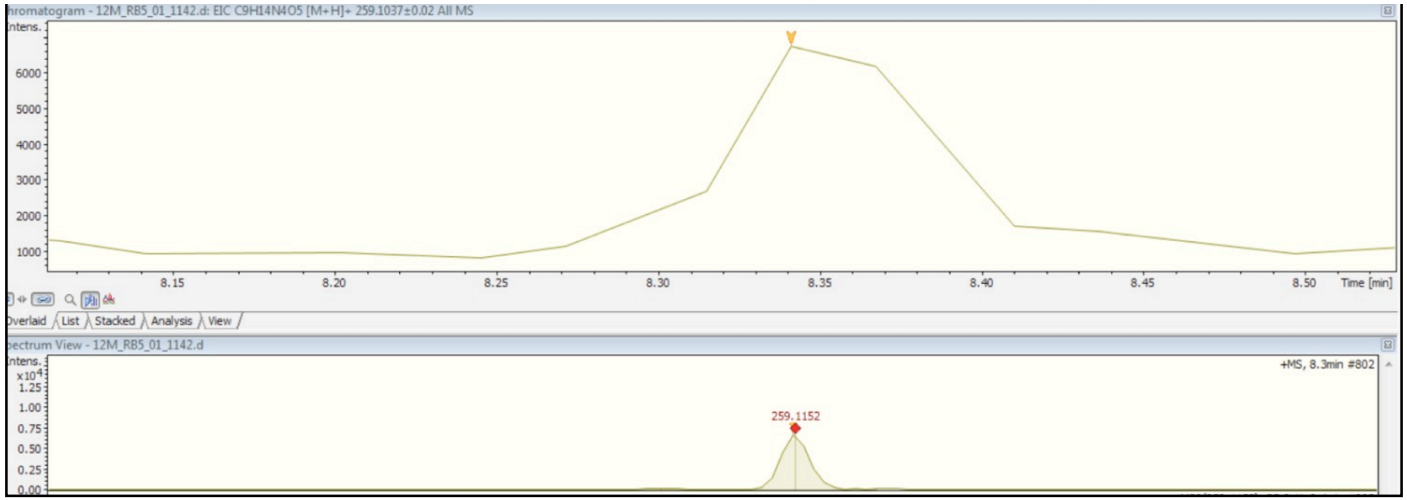


Figure 12. A new AMP-activated protein (AMPK) activator (Acadesine) found in *Anacardium Occidentale* (12M).

A-769662 is a new activator of AMP-activated protein kinase (AMPK). It had been proven that A-769662 stimulated AMPK release and inhibited fatty acid synthesis in mice. It is a feasible candidate for the treatment of T2DM and metabolic syndrome.

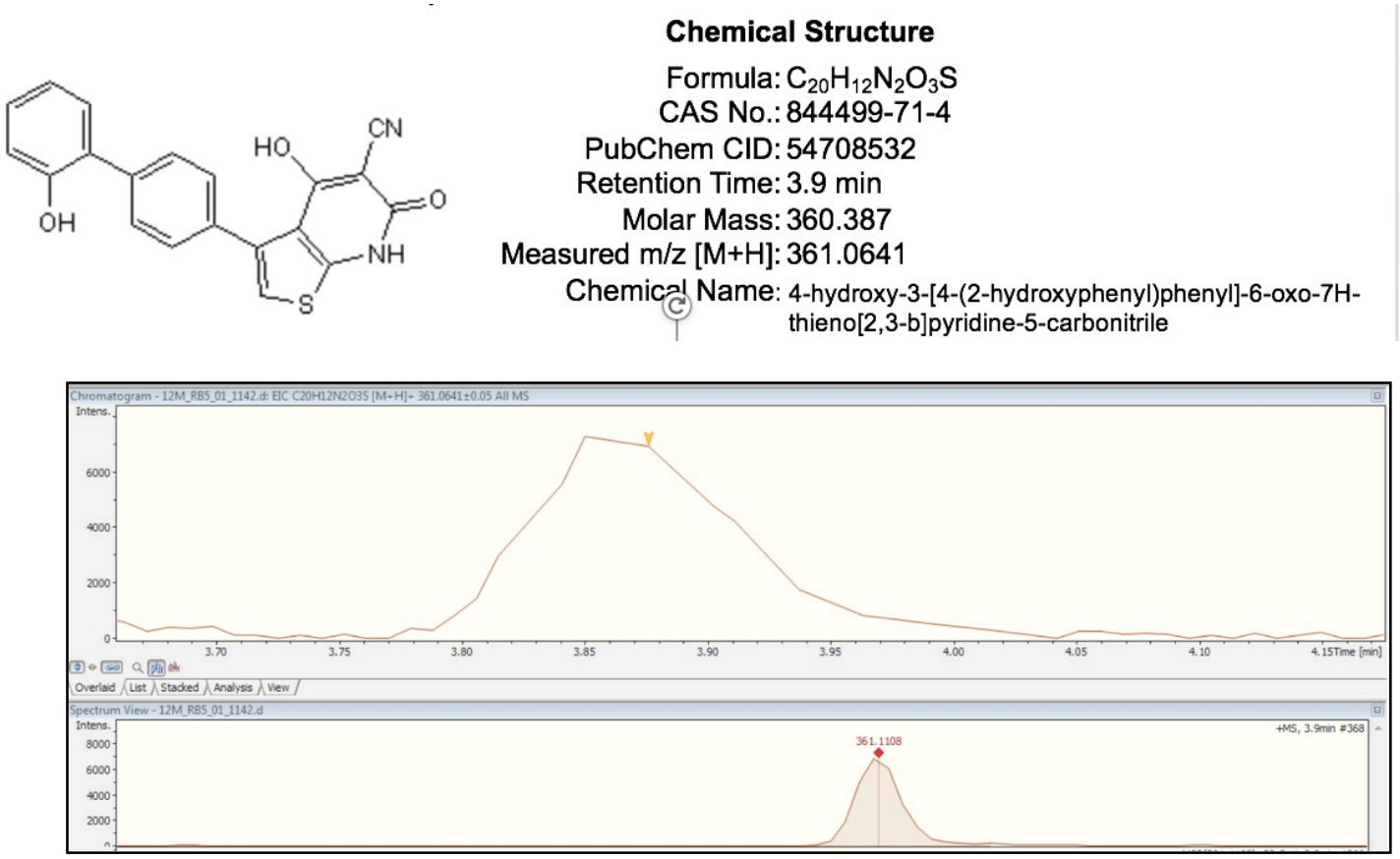
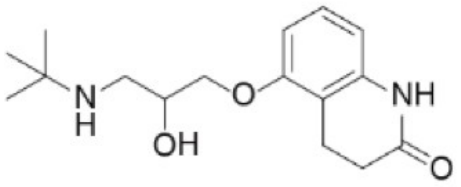


Figure 13. A new AMP-activated protein (AMPK) activator (A-769662) found in *Anacardium Occidentale* (12M).

Carteolol is a non-selective β-adrenergic antagonist used for the treatment of arrhythmia, angina, hypertension and glaucoma.



Chemical Structure

Formula: $C_{16}H_{24}N_2O_3$
CAS No.: 51781-06-7
PubChem CID: 2583
Retention Time: 2.2 min
Molar Mass 292.3734
Measured m/z [M+H]: 293.1860
Chemical Name: 5-[3-(tert-butylamino)-2-hydroxypropoxy]-3,4-dihydro-1H-quinolin-2-one

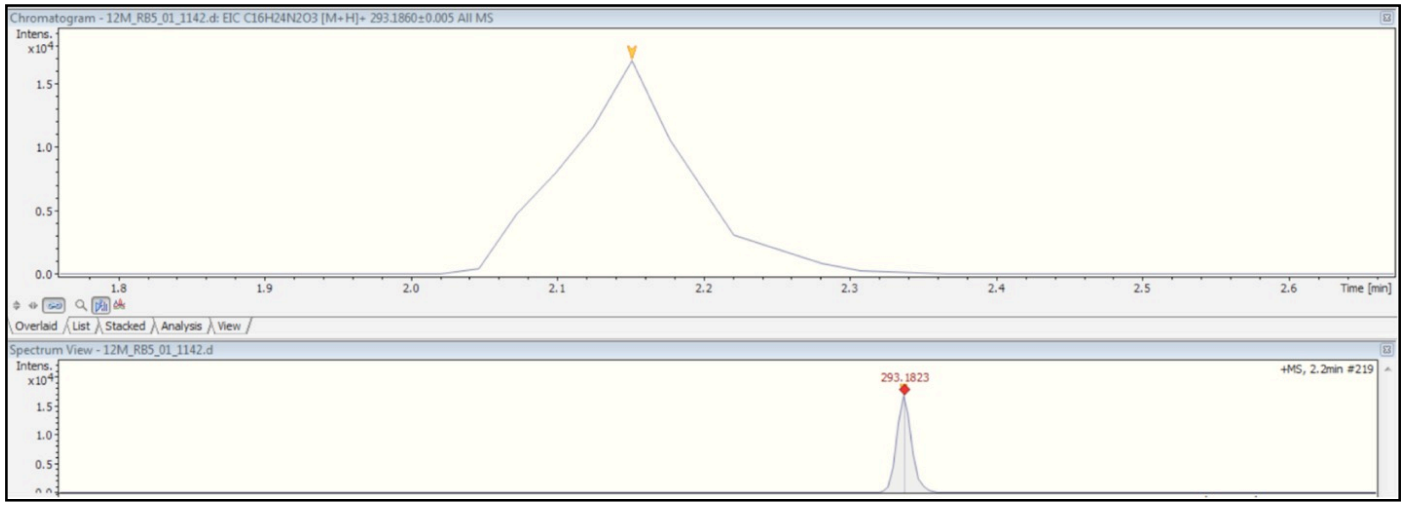
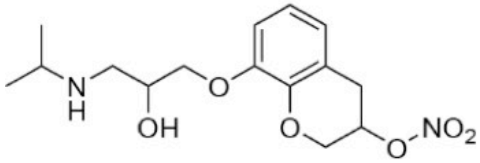


Figure 14. A β-blocker anti-hypertensive agent (Carteolol) found in *Anacardium Occidentale* (12M).

Nipradilol is a non-cardioselective β-blocker used for hypertension management which is approved in Japan.



Chemical Structure

Formula: $C_{15}H_{22}N_2O_6$
CAS No.: 0081486-22-8
PubChem CID: 72006
Retention Time: 11.1 min
Molar Mass: 326.349
Measured m/z [M+H]: 327.1551
Chemical Name: 8-[2-hydroxy-3-(propan-2-ylamino) propoxy]-3,4-dihydro-2H-chromen-3-yl] nitrate

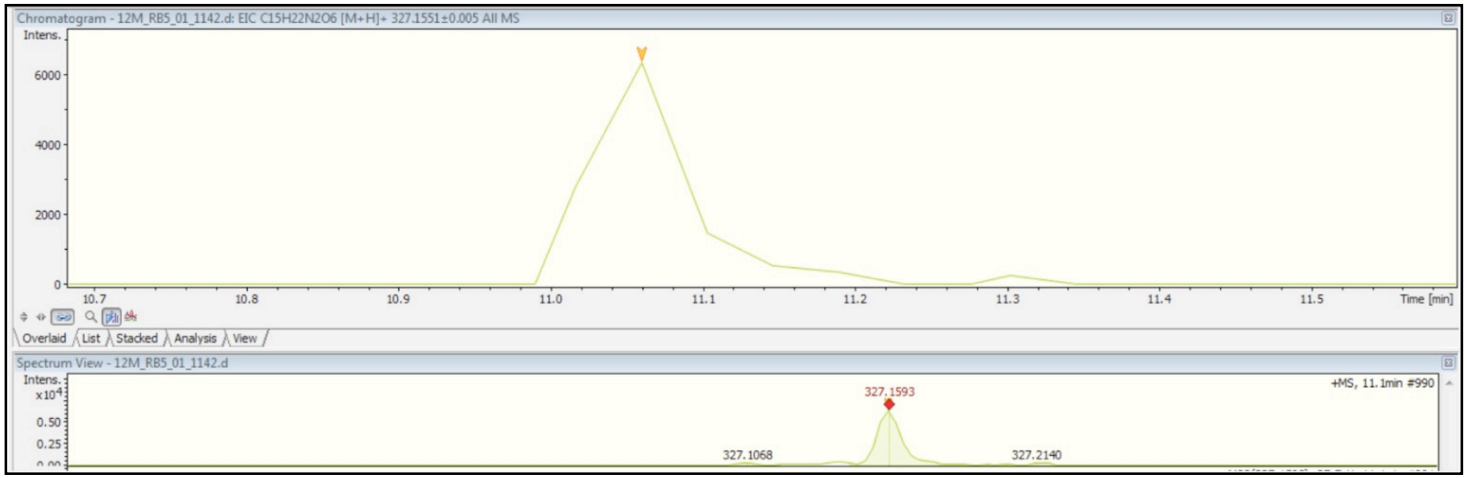
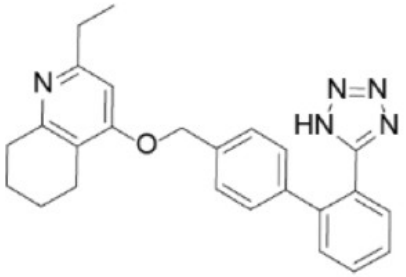


Figure 15. A non-cardioselective β-blocker (Nipradilol) found in *Anacardium Occidentale* (12M)

ZD-6888 is an Angiotensin-Receptor blocker (ARB) used for the treatment of hypertension. However, the research has been discontinued.



Chemical Structure

Formula: $C_{25}H_{25}N_5O$
PubChem CID: 9887844
Retention Time: 9.6 min
Molar Mass: 411.509
Measured m/z [M+H]: 412.2132
Chemical Name: 2-ethyl-4-[[4-[2-(2H-tetrazol-5-yl)phenyl]phenyl]methoxy]-5,6,7,8-tetrahydroquinoline

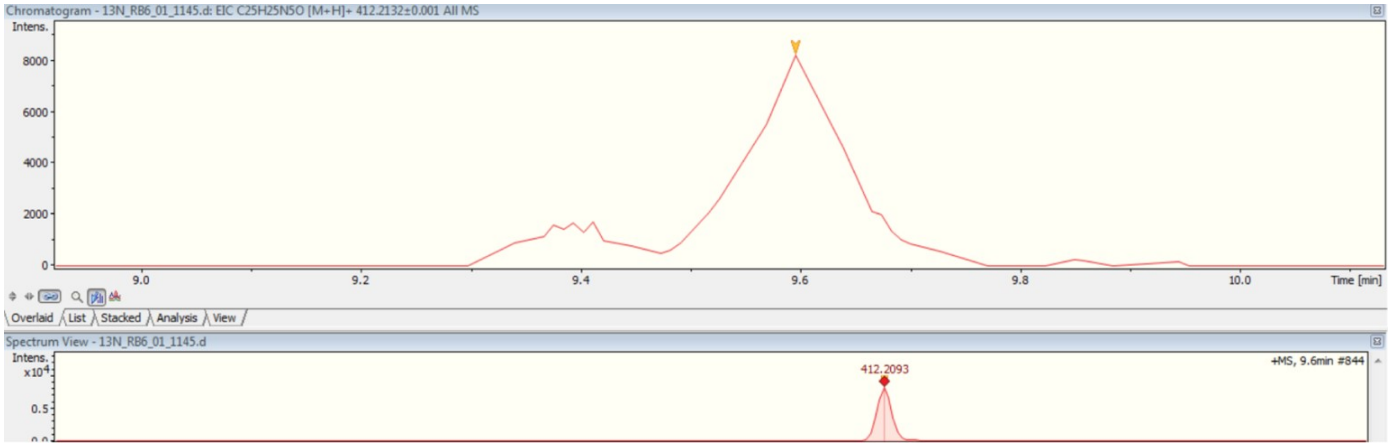


Figure 16. An Angiotensin-Receptor blocker (ZD-6888) for the hypertension management found in *Moringa Oleifera* (13M).

12. Table

Catalog	Classification	Total Numbers of Agents	Positive Results
Anti-diabetic Agents	6	92	5
Anti-hypertensive Agents	5	170	3
Anti-obesity Agents	--	34	--

Table 1. The summary of in-house Drug Library.

Anti-diabetic Agents	Description	Drugs	Results		
			11L	12M	13N
Dipeptidyl-peptidase-4 (DPP-4) Inhibitors	DPP-4 inhibitors are a class of oral anti-diabetic agents that block dipeptidyl peptidase-4 (DPP-4). They can be used to the management of T2DM.	34	1 (+) $C_{15}H_{18}N_6O$	(-)	(-)
Sodium/Glucose co-transporter 2 (SGLT-2) Inhibitors	SGLT-2 Inhibitors block reabsorption of glucose in kidney to reduce glucose level in blood.	16	(-)	(-)	(-)
Sulfonylureas	Sulfonylureas facilitate insulin release and increase insulin sensitive of beta cells in the pancreas	16	1 (+) $C_{15}H_{20}N_2O_4S$	1 (+) $C_{15}H_{20}N_2O_4S$	(-)
Adenosine 5'-monophosphate Active Protein kinase (AMPK) Activators	AMPK is a central regulator of energy homeostasis, which increase glucose uptake, reduce cholesterol synthesis, and facilitate fatty acid catabolism by various metabolic pathways	9	(-)	2(+) $C_{20}H_{12}N_2O_3S$ $C_9H_{14}N_4O_5$	(-)
Peroxisome Proliferator-Activated Receptors (PPARs) Agonist	They used for the treatment of the metabolic syndrome to regulate glucose homeostasis and increase fatty acid oxidation.	11	(-)	(-)	(-)
Alpha Glucosidase Inhibitors	Alpha-glucosidase inhibitors are oral anti-diabetic drugs used for T2DM that work by preventing the digestion of carbohydrates.	6	1(+) $C_{10}H_{21}NO_7$	1(+) $C_{10}H_{21}NO_7$	(-)

Table 2. The summary of identified anti-diabetic agents (compounds)/(+)- in plants extraction.

Anti-hypertensive Agents	Description	Drugs	Results		
			11L	12M	13N
Angiotensin-Converting- Enzyme (ACE) Inhibitors	Angiotensin-converting-enzyme inhibitor (ACE inhibitor) is primarily for the treatment of hypertension and heart failure. And it is also useful to kidney diseases including kidney complication of diabetes mellitus.	28	(-)	(-)	(-)
Angiotensin-Receptor Blockers (ARBs)	Angiotensin II receptor blockers (ARBs) are a group of pharmaceuticals to treatment of hypertension, diabetic nephropathy (kidney damage due to diabetes) and congestive heart failure.	29	(-)	(-)	1 (+) $C_{25}H_{25}N_5O$
Adrenergic Blockers	β-Blocker are class of medications that are particularly used to manage abnormal heart rhythms and heart attack. β - Blocker can reduce the risk of cardiovascular events and death in post myocardial infarction patients with diabetes.	78	(-)	2(+) $C_{15}H_{22}N_2O_6$ $C_{16}H_{24}N_2O_3$	(-)
Thiazide Diuretics	Thiazide diuretics are the class of medications to treat hypertension and congestive heart failure as well as the accumulation of fluid and swelling of the body caused by heart failure, chronic kidney failure and nephrotic syndrome.	13	(-)	(-)	(-)
Calcium-Channel Blockers (CCBs)	CCB is a class of drug to disrupt the movement of calcium through calcium cannels. It is commonly used as anti- hypertensive drugs.	22	(-)	(-)	(-)

Table 3. The summary of identified anti-hypertensive agents (compounds)/(+)- in plants extraction.

13. Figures

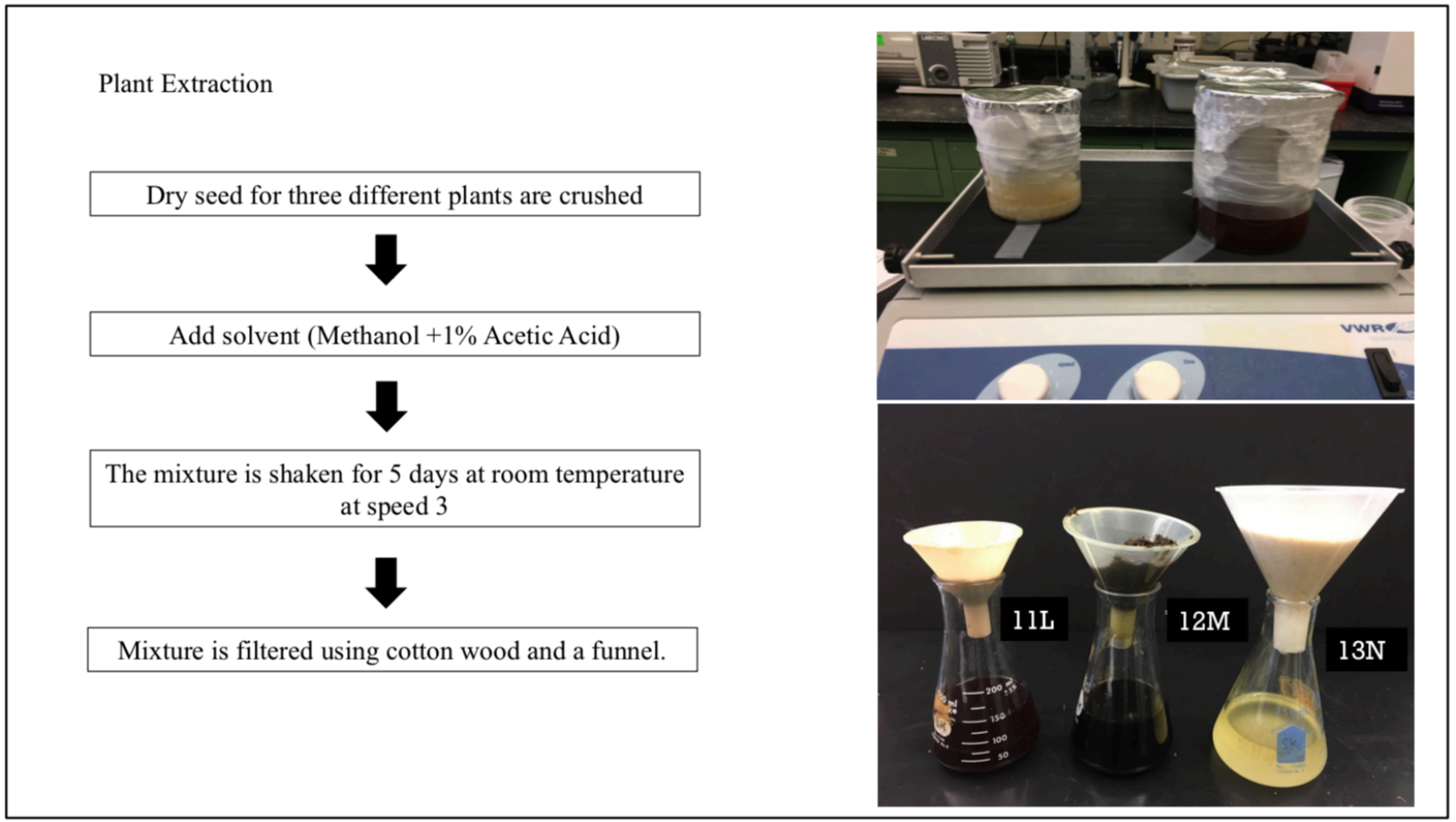


Figure 1. The method of compound extraction.

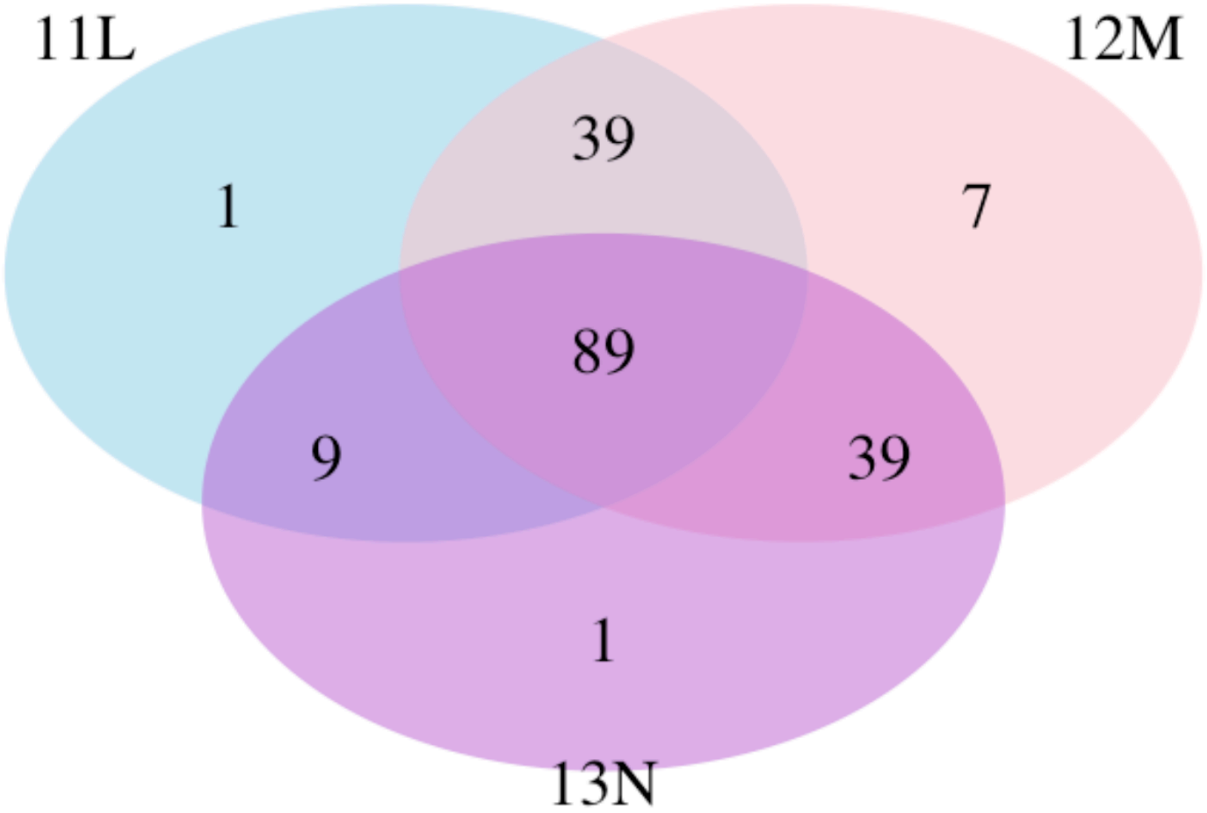


Figure 2. A venn diagram of identified compound of extraction of *Khaya Senegalensis* (11L), *Anacardium Occidentale* (12M), and *Moringa Oleifiera* (13M)

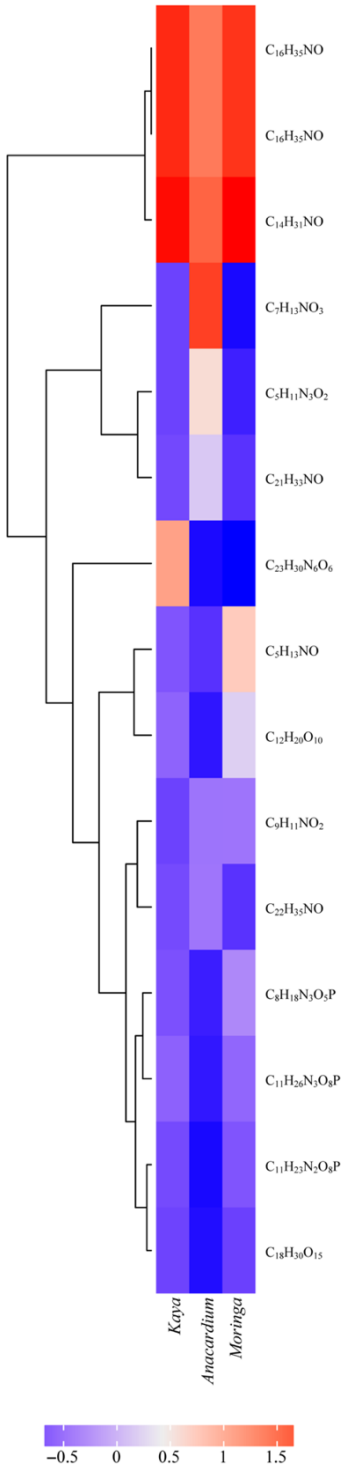


Figure 3. Heat map for identified compound (cluster 1-High-Intensity)

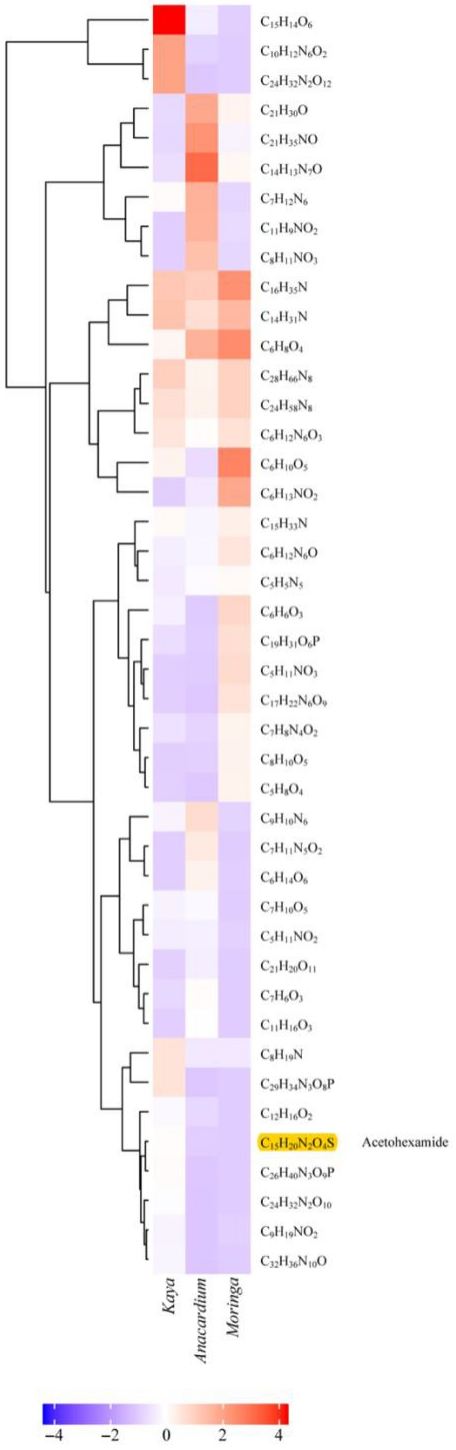


Figure 4. Heat map for identified compound cluster 2 (Identified drug is highlighted)

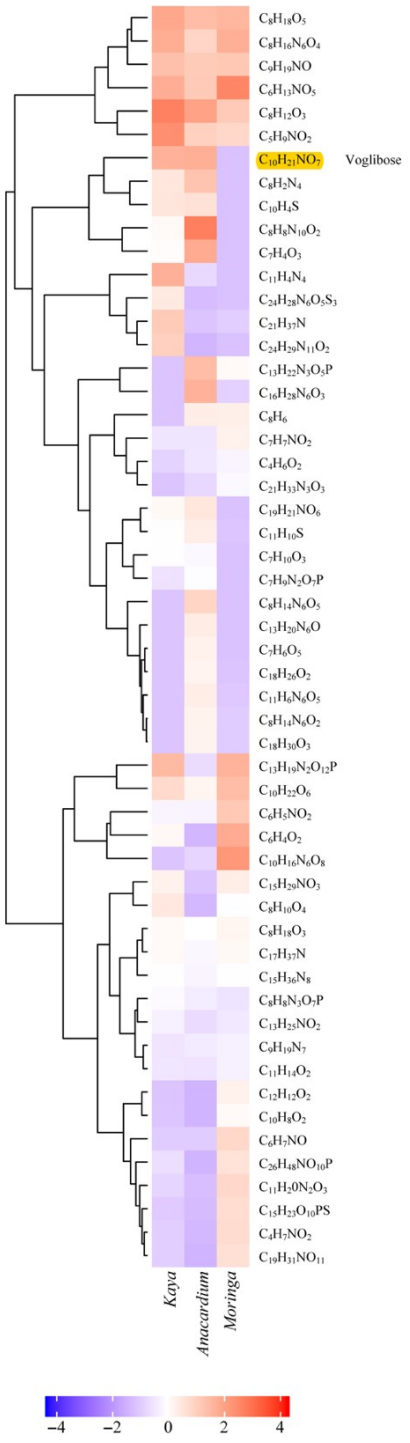


Figure 5. Heat map for identified compound cluster 3 (Identified drug is highlighted)

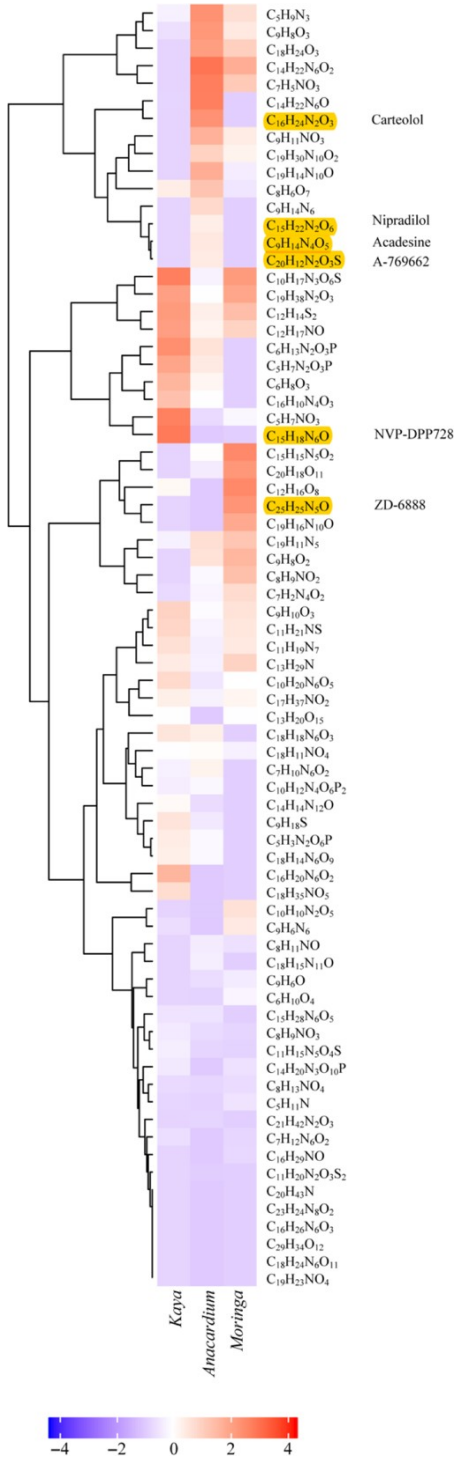
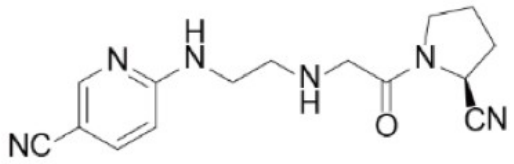


Figure 6. Heat map for identified compound cluster (Low intensity)
(Identified drug is highlighted)

NVP-DPP728 is a dipeptidyl peptidase-4 (DPP-4) inhibitor for the T2DM treatment developed by Novartis.



Chemical Structure

Formula:	$C_{15}H_{18}N_6O$
CAS No.:	247016-69-9
PubChem CID:	9796290
Retention Time:	18.2 min
Molar Mass:	298.34
Measured m/z [M+H]:	299.1615
Chemical Name:	6-[[2-[[2-(2S)-2-Cyano-1-pyrrolidinyl]-2-oxoethyl]amino]ethyl]amino-3-pyridinecarbononitrile

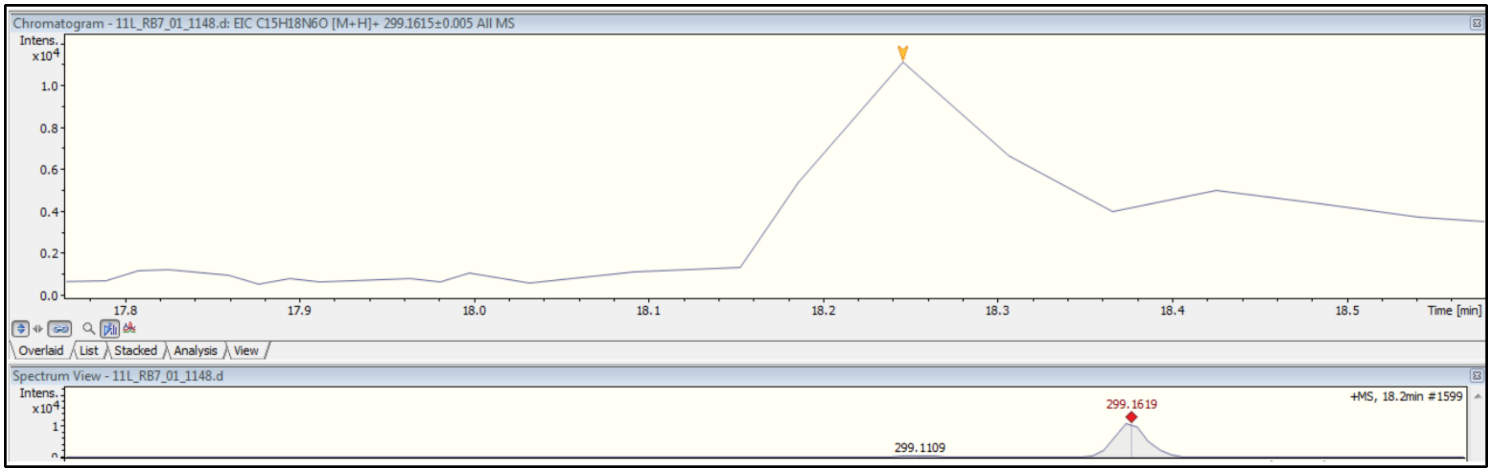
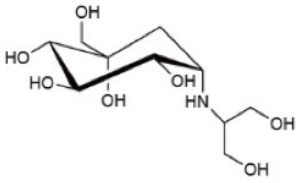


Figure 7. A DPP-4 Inhibitor (NVP-DPP728) found in *Khaya Senegalensis*.

Voglibose is an α-glucosidase inhibitor used for lowering post-prandial blood glucose levels in people with diabetes mellitus by preventing the digestion of complex carbohydrates. Voglibose was approved in Japan in 1994.



Chemical Structure

Formula:	$C_{10}H_{21}NO_7$
CAS No.:	83480-29-9
PubChem CID:	444020
Retention Time	7min
Molar Mass:	267.2762
Measured m/z [M+H]:	268.1391
Chemical Name:	1S,2S,3R,4S,5S)-5-(1,3-dihydroxypropan-2-ylamino)-1-(hydroxymethyl) cyclohexane -1,2,3,4-tetrol

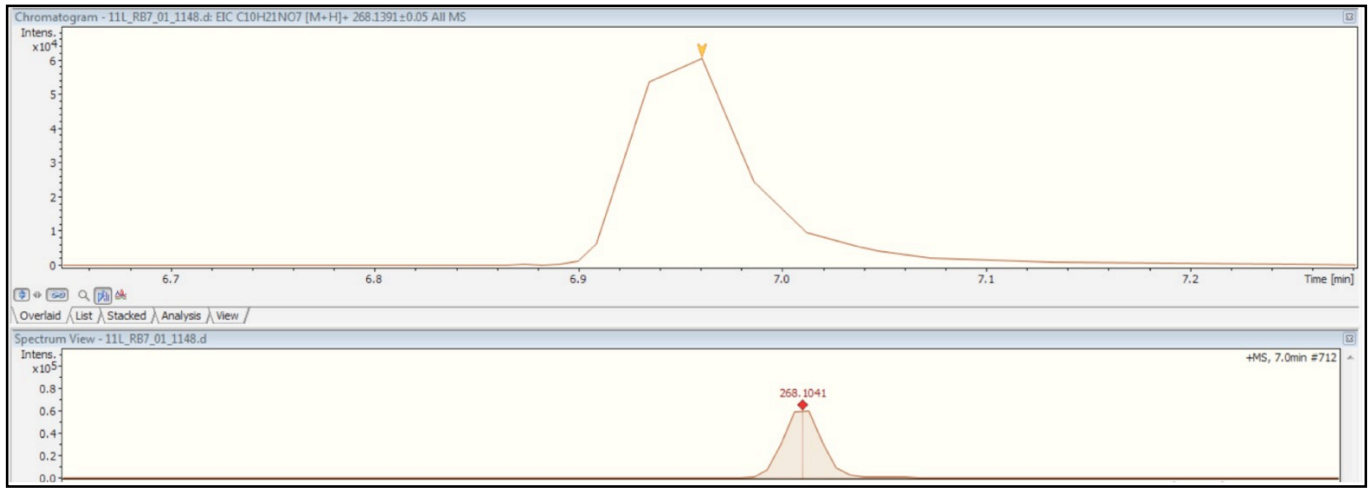
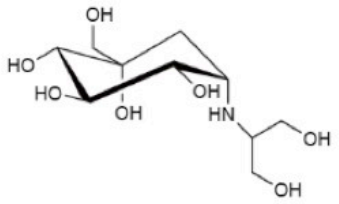


Figure 8. A α-glucosidase inhibitor (Voglibose) found in *Khaya Senegalensis* (11L).

Voglibose is an α-glucosidase inhibitor used for lowering post-prandial blood glucose levels in people with diabetes mellitus by preventing the digestion of complex carbohydrates. Voglibose was approved in Japan in 1994



Chemical Structure

Formula:	$C_{10}H_{21}NO_7$
CAS No.:	83480-29-9
PubChem CID:	444020
Retention Time	7min
Molar Mass:	267.2762
Measured m/z [M+H]:	268.1391
Chemical Name:	1S,2S,3R,4S,5S)-5-(1,3-dihydroxypropan-2-ylamino)-1-(hydroxymethyl) cyclohexane -1,2,3,4-tetrol

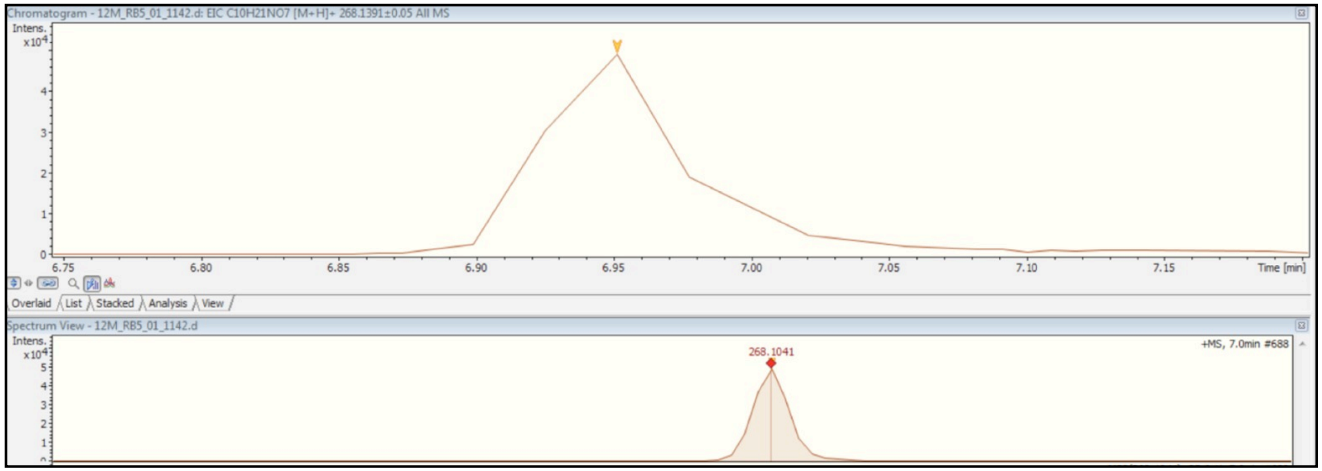
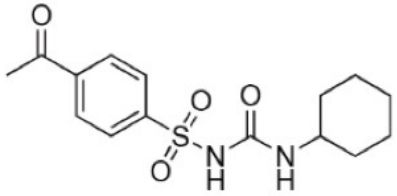


Figure 9. A α-glucosidase inhibitor (Voglibose) found in *Anacardium Occidentale* (12M).

Acetohexamide is the first-generation oral sulfonylurea for T2DM management, which stimulates β-cells to secrete more insulin and increase insulin sensitivity. However, Acetohexamide has been discontinued in the US market.



Chemical Structure

Formula: $C_{15}H_{20}N_2O_4S$
CAS No.: 968-81-0
PubChem CID: 1989
Retention Time: 2.7 min
Molar Mass: 324.395
Measured m/z [M+H]: 325.1217
Chemical Name: 1-((p-Acetylphenyl)sulfonyl)-3-cyclohexylurea

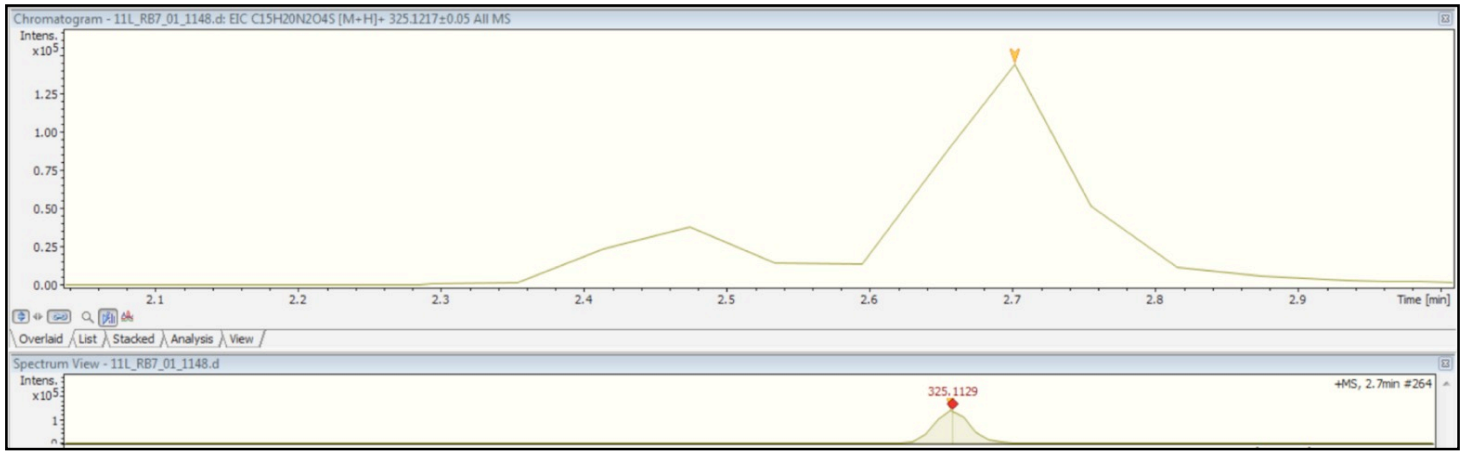
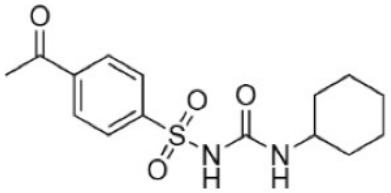


Figure 10. A first-generation sulfonylurea (Acetohexamide) found in *Khaya Senegalensis* (11L).

Acetohexamide is the first-generation oral sulfonylurea for T2DM management, which stimulates β-cells to secrete more insulin and increase insulin sensitivity. However, Acetohexamide has been discontinued in US market.



Chemical Structure

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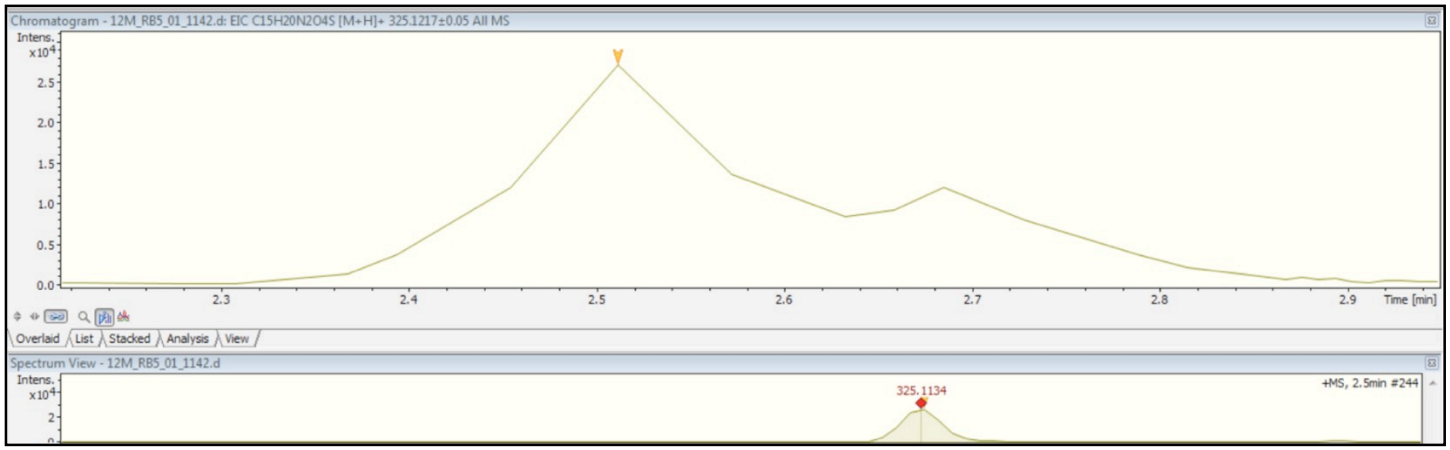
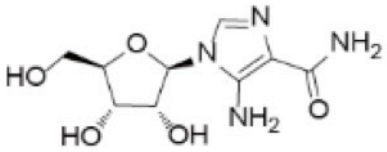


Figure 11. A first-generation sulfonylurea (Acetohexamide) found in *Anacardium Occidentale* (12M).

Acadesine is an AMPK activator for the treatment of impaired glucose tolerance, insulin resistance in both T1DM and T2DM with poor oral bioavailability, which limited its application.



Chemical Structure

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CAS No.: 844499-71-4
PubChem CID: 2627-69-2
Retention Time: 8.3 min
Molar Mass: 258.234
Measured m/z [M+H]: 259.1037
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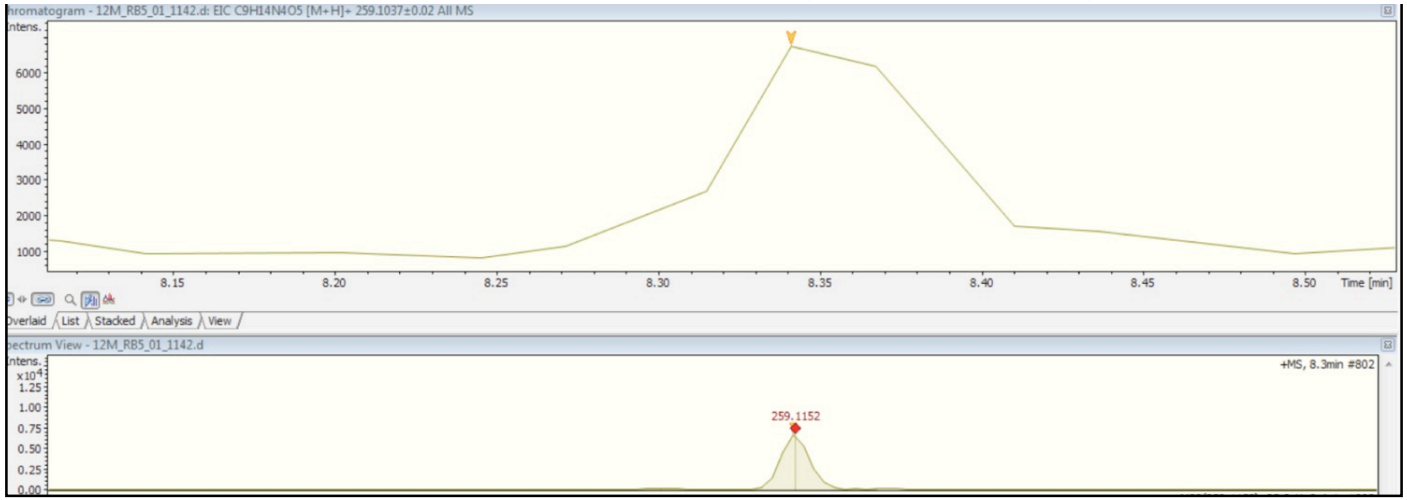

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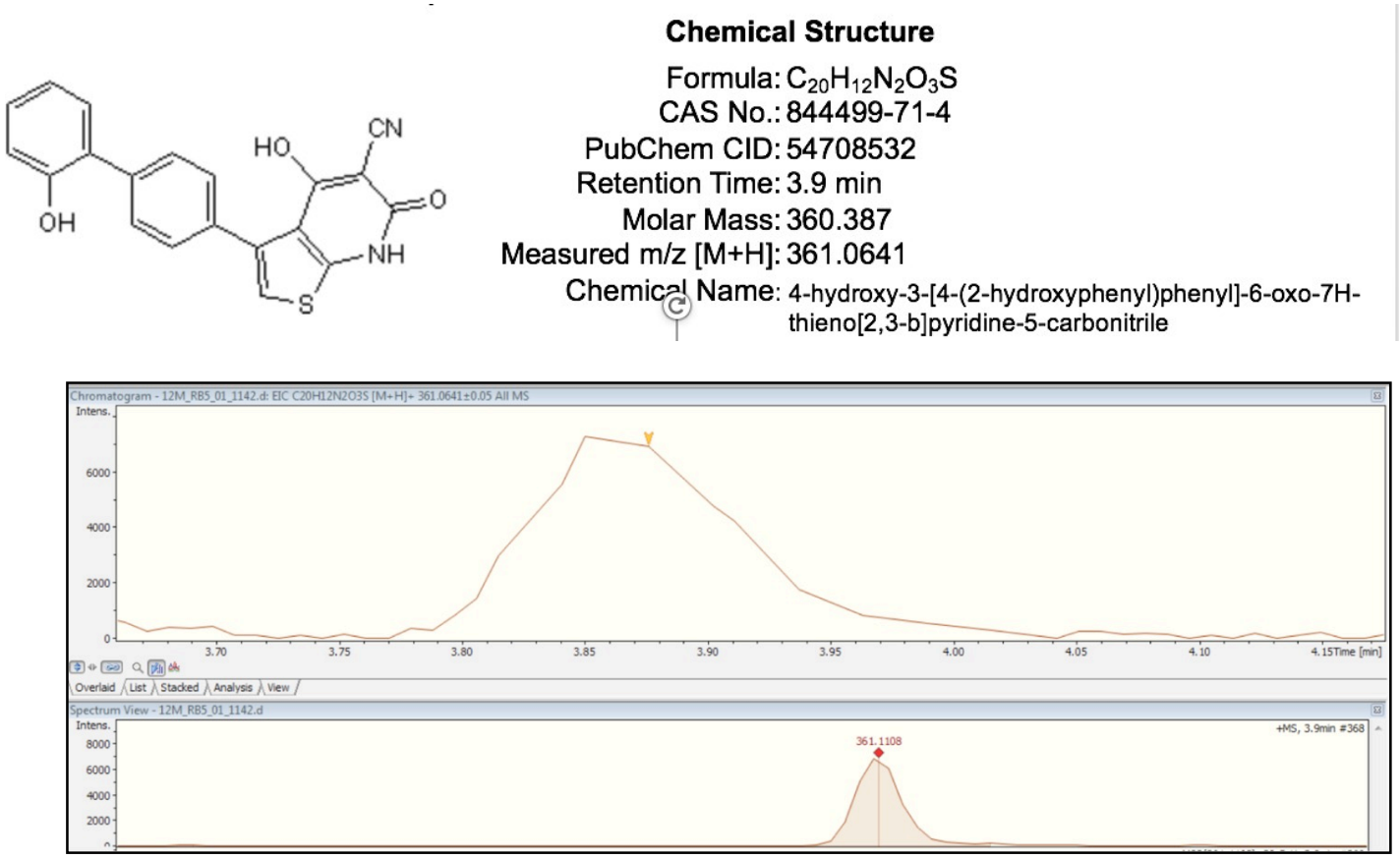
A-769662 is a new activator of AMP-activated protein kinase (AMPK). It had been proven that A-769662 stimulated AMPK release and inhibited fatty acid synthesis in mice. It is a feasible candidate for the treatment of T2DM and metabolic syndrome.



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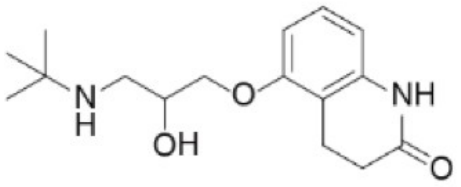


Chemical Structure

Formula: $C_{16}H_{24}N_2O_3$
CAS No.: 51781-06-7
PubChem CID: 2583
Retention Time: 2.2 min
Molar Mass 292.3734
Measured m/z [M+H]: 293.1860
Chemical Name: 5-[3-(tert-butylamino)-2-hydroxypropoxy]-3,4-dihydro-1H-quinolin-2-one

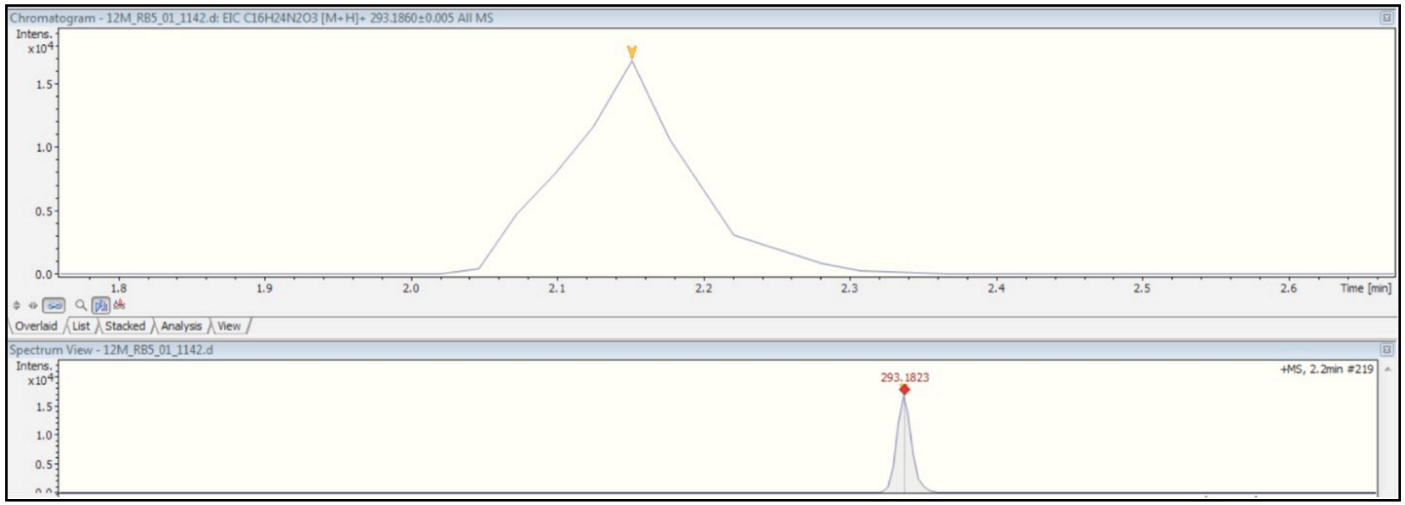
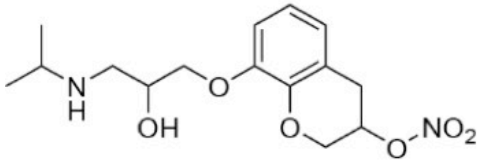


Figure 14. A β-blocker anti-hypertensive agent (Carteolol) found in *Anacardium Occidentale* (12M).

Nipradilol is a non-cardioselective β-blocker used for hypertension management which is approved in Japan.



Chemical Structure

Formula: $C_{15}H_{22}N_2O_6$
CAS No.: 0081486-22-8
PubChem CID: 72006
Retention Time: 11.1 min
Molar Mass: 326.349
Measured m/z [M+H]: 327.1551
Chemical Name: 8-[2-hydroxy-3-(propan-2-ylamino) propoxy]-3,4-dihydro-2H-chromen-3-yl] nitrate

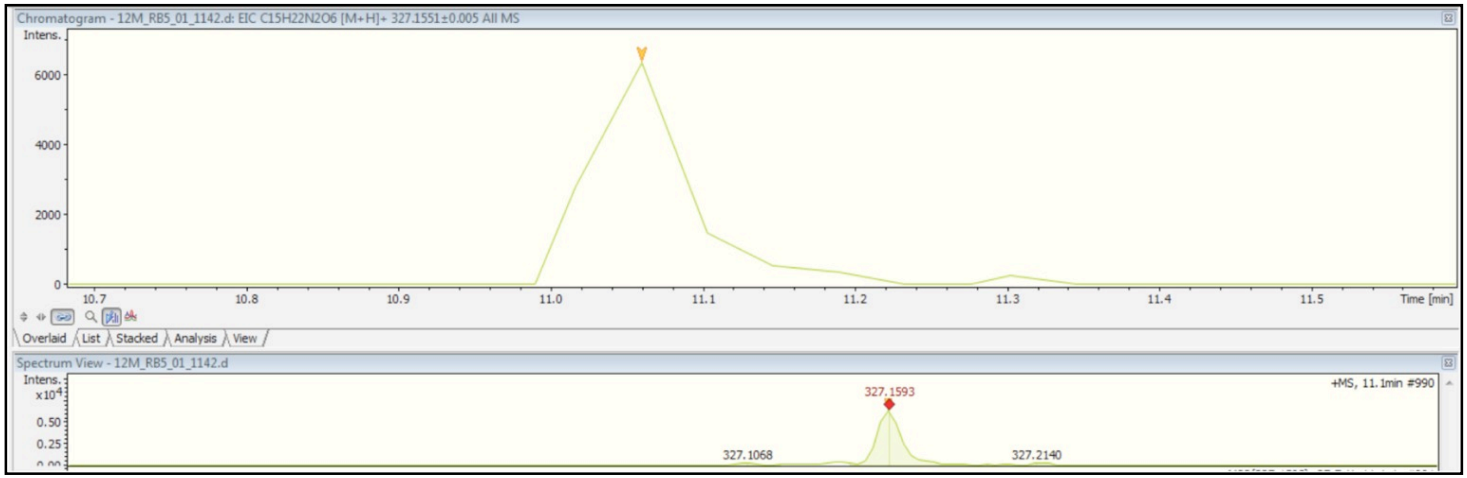
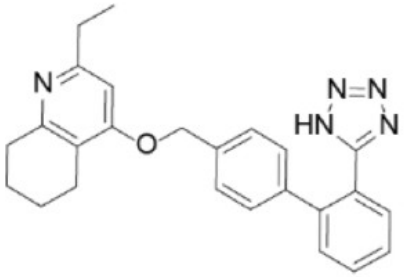


Figure 15. A non-cardioselective β-blocker (Nipradilol) found in *Anacardium Occidentale* (12M)

ZD-6888 is an Angiotensin-Receptor blocker (ARB) used for the treatment of hypertension. However, the research has been discontinued.



Chemical Structure

Formula: $C_{25}H_{25}N_5O$
PubChem CID: 9887844
Retention Time: 9.6 min
Molar Mass: 411.509
Measured m/z [M+H]: 412.2132
Chemical Name: 2-ethyl-4-[[4-[2-(2H-tetrazol-5-yl)phenyl]phenyl]methoxy]-5,6,7,8-tetrahydroquinoline

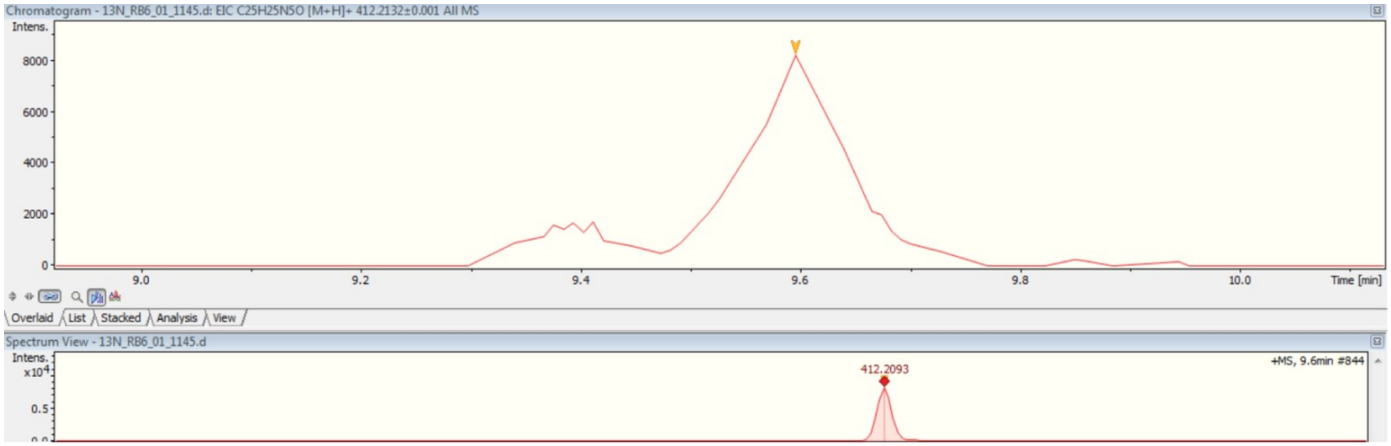


Figure 16. An Angiotensin-Receptor blocker (ZD-6888) for the hypertension management found in *Moringa Oleifera* (13M).

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