# Medicinal Plants in Asia for Metabolic Syndrome

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## Natural Products and Molecular Basis



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# *Dedication*

*If we want real peace in this world, we should start educating children.*

**Mahatma Gandhi**

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# Foreword I

Metabolic syndrome is manifested as elevated fasting blood glucose level, increase in triglyceride level in blood, abdominal obesity, low high-density lipoprotein cholesterol, and high blood pressure. It poses high health risk to humans and is a major predisposing factor for life-threatening disorders such as type 2 diabetes, cardiovascular diseases, and cancer. Concerning its prevalence, the International Diabetes Federation estimates that one-quarter of the world's population has developed metabolic syndrome, and 20% of adults in the Western world have developed metabolic syndrome. Natural products obtained from terrestrial plants, marine organisms, and microorganisms have been successfully harnessed in providing therapeutic agents as well as drug leads for an array of illnesses. Furthermore, natural products have long been a source of prophylactic medicines/preventive remedies, particularly against metabolic disorders. A large number of traditional herbs have proven effective as antimetabolic syndrome medicines in animal models and humans. A myriad of phytochemicals (from different classes such as flavonoids, phenylpropanoids, phenylheptanoids, xanthones, and other polyphenols), steroids, organosulfur compounds, and alkaloids have reportedly exhibited the ability to reduce hyperglycemia, attenuate hypertension, lower hyperlipidemia, and help weight control. Molecular mechanisms involved in the prevention of the metabolic syndrome include antioxidant and anti-inflammatory actions, modulation of key signal transduction cascades, glucose transport, inhibition or stimulation of enzymatic activity, regulation of mitochondrial function, modulation of protein expression, and regulation of transcription factors, in addition to other mechanisms of action. Exploitation of natural products against metabolic syndrome and the associated diseases has been the subject of extensive investigations over the past few decades and currently witnesses growing interest.

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# Foreword II

Metabolic syndrome is known for a cluster of conditions—hypertension, elevated blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels—that occur together, thus increasing oxidative stress and increasing the probability of heart disease, stroke, and diabetes. It is closely linked to overweight or obesity and inactivity. In recent times, the number of people affected with metabolic syndrome is rising at an alarming rate. According to the World Health Organization estimates for 2014, there are 600 million clinically obese and 1.9 billion overweight adults worldwide, and there are more than 415 million people with diabetes. Allopathic medicines cannot cure but merely offer symptomatic relief. Moreover, such medicines are costly and not available or affordable to the poorer sections of the population of a country or people residing in remote regions. Some conditions such as arterial blockages (which can result from high cholesterol and lead to stroke) may need surgery, which is expensive and substantially decreases the quality of lifestyle of the patient. Despite an array of medications to decrease blood sugar levels, there are no medications through which diabetes can be cured. This disease, with the progress of time, can lead to further complications such as cardiovascular disorders, diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy. As such, effective medicines to treat metabolic syndrome is a necessity and cries for attention from scientists.

Plants have always been a source for new and effective drugs. Apart from Brazil, the various countries of Asia in between them contain a huge number of diverse floristic species. These species, most of which remain unexplored from the pharmacological point of view, contain thousands of phytochemicals, which need to be researched as potential sources of new drugs. From that viewpoint, this book is exceptional. Dr. Christophe Wiart has done a magnificent job in exploring the vast medicinal plant wealth of Asia toward identifying possible plants and their secondary metabolites along with their mechanism of action, which can be of immense benefit to scientists and researchers, and help find possible drugs against metabolic syndrome.

Using plants for curing or alleviating metabolic syndrome is a concept that dates back possibly thousands of years ago. The ancient Indian system of medicine, Ayurveda, describes a set of complex clinical disorders, collectively called Prameha, that are characterized by frequent abnormal micturition. The clinical conditions as described in ancient Ayurvedic texts for Prameha correlate in many ways with obesity, metabolic syndrome, and diabetes mellitus. A number of plant-based monoherbal and polyherbal formulations are used in Ayurveda to treat Prameha. However, it cannot be denied that more effective medicines may be essential to treat metabolic syndrome than those that are available in Ayurveda for treatment of Prameha, and the active ingredients in these plant-based medicines are identified. Modern-day scientists are recognizing the importance of plants in treating obesity, hypertension, and diabetes either alone or in combination as in metabolic syndrome.

A simple search of recent scientific literature demonstrates a variety of plants, which are reportedly active against metabolic syndrome or at least some of its symptoms. *Cissus quadrangularis*, a common plant in the Indian subcontinent but also found in other Asian countries, also known as veldt grape in English, is more known for its bone fracture healing abilities. However, recent research has shown that the plant can reduce weight as well as improve blood parameters associated with metabolic syndrome. Red orange juice has proved effective in reducing insulin resistance and systolic blood pressure. Tea, prepared from the leaves of *Camellia sinensis*, has been shown to reduce body weight, alleviate metabolic syndrome, and prevent diabetes and cardiovascular diseases in animal models and humans. Grapes and particularly grape seeds have proved effective in inhibiting hyperlipidemia, hyperglycemia, and hypertension. Plants such as red ginseng or *Hibiscus sabdariffa*, *Rosmarinus officinalis*, and *Hylocereus polyrhizus*, to name only a few, have also shown efficacy against metabolic syndrome. The evidences already present in the scientific literature suggest two things: (1) plants may prove to be the effective remedy against metabolic syndrome and

(2) possibly polyherbal formulations will be necessary to treat the multiple disorders present in metabolic syndrome more effectively.

It is in this context that this book gains importance. The large number of plants discussed in the book can make scientific studies more relevant and also enable potential scientists to combine plants in a manner to treat metabolic syndrome more effectively without any adverse effects from interaction between the various plants that may be used. Thus, the book is not only useful to scientists and researchers, but also to the average persons in knowing more about this metabolic disorder affecting human beings.

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# Foreword III

In this rapidly changing world there are always new challenges for production of food, drug, and also for health care at large. Natural products play a major role in health care throughout the globe. Several governments of individual countries and international organizations have advocated the use of traditional medicines in primary health care. This should be more effective when the evidences for use of those traditional medicines are being documented scientifically, which is an urgent need for evidence-based validation of traditional medicines to make them available for the treatment of a large community.

In Asian region, the traditional knowledge has been recorded in books or old scriptures that are thousand years old but still plays an important role in health care. This has led to the development of several new approaches supported with the new economic realities. Ayurveda is one of the holistic health care systems, which has been recognized as an ancient science of life.

बहुता तत्रयोग्यत्वमनेकविधकल्पना|
सम्पच्चेति चतुष्कोऽयं द्रव्याणां गुण उच्यते||

(च .सू– ९/७)
**[Devanagari Script]**

**Bahuta tatrayogyatwamanekvidh kalpana |**
**Sampaaccheti chatushkoayam dravyanam guna uchhyate ||**
(***Charka Samhita Sutrasthana*** - 9/7)

**[Diacritical Script]**

*Available in abundance, affectivity, various pharmaceuticals forms, and having appropriate properties are the four qualities of drugs*

*Ayurveda* is getting global acceptance primarily due to its age-old therapeutic practice and profound conceptual basis. The philosophy of treating a system or body as a whole is gaining relevance during transition from reductionist approach to "systems" approach in the post-genomic era. Ayurveda describes obesity as a disease of "medadhatu" (adipose tissue), which leads to hugeness (sthoulyam) and referred as "medoroga." Chikitsa (therapy) for obesity comprised of elimination of nature's waste (purification), dietary composition, energy expenditure, and reduction of hormonal stress with yoga. In Ayurvedic pharmacology, many plants and formulations have been reported for drug interventions in obesity management. Efficacy and potential of Ayurvedic medicines is also evident from many recent scientific publications, for example, study on Ashwagandha (*Withania somnifera*) that lead to the discovery of a novel therapeutic strategy for Alzheimer's disease reversal. Ayurveda, apart from the therapeutic potential also has a predictive, preventive, and personalized approach to health and management of disease, which has been extensively documented in original texts of Charaka and Sushruta Samhita. This potential has not been harnessed effectively in drug-discovery programs.

The metabolic syndrome is a collective term that refers to obesity-associated metabolic abnormalities. There is several health risks associated with obesity. Utilization of plant components and its derived products has a prospective future for controlling the prevalence of metabolic syndrome. Several evidences are exploring to support the use of herbs as an alternative way of obesity control and weight management. Diet-based therapies and herbal supplements are among the most common complementary and alternative medicine modalities for weight loss. A large number of populations in Asia depend on traditional practitioners and their prescription of medicinal plants to assemble

health care needs. Hence, it is really obvious that plants may offer an efficient option for the treatment of metabolic syndrome.

For commercialization of botanical products, the assurance of safety, quality, and efficacy of medicinal herbs and botanical products has become an important issue. The regulations of several countries including the National Centre for Complementary and Alternative Medicine, Bethesda, Maryland, and WHO stress the importance of qualitative and quantitative methods for characterizing botanical samples, quantification of the biomarkers and/or chemical markers, and the fingerprint profiles. Different approaches can be used for chemical standardization such as pretreatment that involves drying and grinding; selection of a suitable method of extraction; analysis of compounds using suitable chromatographic or spectroscopic methods; the analysis of data based on bioactive or marker compounds; quality control; elucidation of the properties of absorption distribution metabolism excretion (ADME) and metabolomics evaluation of medicinal plants. In addition, there is a need to develop scientific proof and clinical validation with chemical standardization, biological assays, animal models, and clinical trials for botanicals.

There has been a global increase in the prevalence of chronic and complex diseases with many lifestyle disorders. Majority of chronic diseases require lifetime medications and in many cases, resistance to drugs is a common problem. Most of the diseases are multifactorial involving complex interplay of a network of genes and nongenetic environmental factors. It is being realized that we need to evolve a systems'-based approach for comprehensive understanding of biology and move toward a network approach in medicine. With the advent of genomics, drug discovery and development program are targeting on the understanding of disease biology in target identification and also aspires to identify responder populations.

This book *Medicinal Plants in Asia for metabolic Syndrome: Natural Products and Molecular Basis* highlights several aspects on the use of the medicinal plants of Asia that are useful in metabolic syndrome particularly against obesity, type 2 diabetes, hypertension, vascular dysfunction, and hyperlipidemia. I appreciate the efforts of Dr. Christophe Wiart for compiling this document, which I am sure will be useful for the researchers and the users of natural medicines to go further with their therapeutic potentials.

**Pulok K. Mukherjee**
*Jadavpur University*

# Preface

Humans lived on earth by hunting animals and gathering plants for food for about 90,000 years. Only recently, have they been exposed to industrial food, urbanization, pollution, and lack of physical activity explaining the recrudescence of obesity, type 2 diabetes, cardiovascular diseases, and other noncommunicable pathologies. In parallel, human knowledge on medicinal plants, or what is called materia medica or pharmacognosy, is disappearing. It is in fact looked down as "an obscure subject" by some accreditation boards lobbied by the pharmaceutical industry. The last traditional healers are aging, and there is a dangerous trend to remove the teaching of pharmacognosy from our comptemporary "Schools of Pharmacy." In fact, graduating pharmacy students (soon to be replaced by dispensing machines) in 2017 are not often getting trained on medicinal plants to the point of ignoring what is opium, cumin if not pepper. The current "late capitalist era," as termed by some, favors profitability and aims at financial benefits of huge corporations. In fact, universities are being themselves often transformed into businesses, resulting in a collapse of academic freedom and a dearth of academic elites. Corporations and financial benefits are also responsible for the destruction of our natural environment, exemplified by the eco-genocide caused by palm oil in Southeast Asia. It can be said that, by the end of this century, many of the medicinal plants provided by Mother Nature and their pharmacological potentials would have been vanished by smoke. The pharmaceutical industry being apparently concerned about its financial benefits does not have much interest in medicinal plants. In fact, it can be said with confidence that a biological feedback will soon occur to force the corporations to change their policies. This is sadly exemplified by the emergence of bacterial resistance and the end of the golden age of antibiotics. It seems that we should be able to live longer and healthier, but it is not the case. In Asia, a wealth of medicinal plants, known since the beginning of time, remains practically unused for the well-being of humans. The purpose of this book is to shed light on the pharmacological properties of carefully selected medicinal plants used in Asia in regard to what has been termed "metabolic syndrome." This book is the result of almost 20 years of medicinal plant research conducted in Southeast Asia. It is principally intended to students, researchers, and academics who have interest in the subject of discovering drugs from Asian medicinal plants for the treatment or prevention of the metabolic syndrome. Medicinal plants, natural products, and their mode of activities are being organized into five chapters corresponding to the major sites of the activity in the body. The plants are listed according to the Takhtajan system of plant classification published in 2008, which allows making chemotaxonomic considerations that are useful to understand the pharmacological activity of medicinal plants. Hundreds of carefully selected bibliographical references are provided and the potentials of the most interesting plants are discussed. It is my hope that this book will create some interest in medicinal plant research and contribute to the discovery of new drugs to fight metabolic syndrome. This book was written in very difficult working conditions, and it would have been impossible to complete it without the support, love, and sacrifices of my family, and particularly my mother, Madam Hora Monollor.

**Christophe Wiart**
*University of Nottingham*

# About the Author

**Christophe Wiart** was born in Saint Malo, France. He received his Pharm D from the Faculty of Pharmacy, University of Rennes, Rennes, France, in 1997 and his PhD from University Pertanian Malaysia, Malaysia in 2001. He served as lecturer and later as associate professor at the University of Malaya, Kuala Lumpur, Malaysia, from 2001 to 2007 and is currently associate professor at the University of Nottingham Malaysia Campus, Selangor, Malaysia, where he teaches pharmacy undergraduates and supervises master's and PhD students. Dr. Wiart appeared on HBO's Vice (television series) in season 3, episode 6 (episode 28 of the series) titled "The Post-Antibiotic World & Indonesia's Palm Bomb." This episode aired on April 17, 2015. It highlighted the need to find new treatments for infections that were previously treatable with antibiotics, but are now resistant to multiple drugs. "The last hope for the human race's survival, I believe, is in the rainforests of tropical Asia," said ethnopharmacologist Dr. Christophe Wiart. "The pharmaceutical wealth of this land is immense." He was invited at TedEx on June 4, 2016. He was the guest at "Inside Story" Aljazeera on September 21, 2016, and interviewed by Adrian Finighan about the rise of superbugs and the chemotherapeutic potentials of medicinal plants in Asia. Dr. Wiart has authored more than 80 publications and 11 academic books on the pharmacological potentials of medicinal plants in Asia. He is the general secretary of the Asian Society of Pharmacognosy and the editor in chief of the *Asian Journal of Pharmacognosy*.

# Introduction

Processed industrial "foods" and "drinks" are associated with noncommunicable diseases of which obesity, the prevalence of which has more than doubled since 1980.[1,2] Simply put, obesity is an accumulation of triglycerides in adipose tissues to the point that the ratio of the body weight (kg) to the height ($m^2$) is equal to or more than 30 $kg/m^2$.[3] Besides ponderal surcharge and aesthetic consideration, visceral adiposity favors the development of insulin resistance, atherogenic dyslipidemia, and hypertension, which are interrelated cardiovascular risk factors collectively referred to as the "metabolic syndrome."[4,5] As for yet, the anti-obesity arsenal is ridiculously limited, and in fact no drug exists yet to efficiently and quickly remove visceral adipose tissues in obese patients who are left with bariatric surgery, strict control of diet, and regular physical exercise. There is therefore a need to develop drugs to prevent or delay the progression of metabolic syndrome in obese patients. In Asia, medicinal plants have been used to treat conditions linked to hyperlipidemia, insulin resistance, type 2 diabetes, hypertension, and cardiovascular diseases since the beginning of mankind, and the systematic pharmacological study of these plants should lead to the discovery of natural products to prevent or manage metabolic syndrome. Today, no single book dedicated to natural products from medicinal plants in Asia for metabolic syndrome exists, and the purpose of this volume is precisely to fill this gap.

## REFERENCES


1. Moodie, R., Stuckler, D., Monteiro, C., Sheron, N., Neal, B., Thamarangsi, T., Lincoln, P., Casswell, S. and Lancet NCD Action Group, 2013. Profits and pandemics: Prevention of harmful effects of tobacco, alcohol, and ultra-processed food and drink industries. *The Lancet*, *381*(9867), 670–679.
2. WHO. Obesity and overweight. 2006. http://www.who.int/mediacentre/factsheets/fs311/en/ (accessed September 2016).
3. Kopelman, P.G., Caterson, I.D. and Dietz, W.H. Eds., 2009. *Clinical Obesity in Adults and Children*. Chichester: John Wiley & Sons.
4. Grundy, S.M., 2008. Metabolic syndrome pandemic. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *28*(4), 629–636.
5. Alberti, K., Eckel, R.H., Grundy, S.M., Zimmet, P.Z., Cleeman, J. and Donato, K., 2009. Harmonizing the metabolic syndrome. A joint interim statement of the IDF Task Force on Epidemiology and Prevention; NHL and Blood Institute; AHA; WHF; IAS; and IA for the Study of Obesity. *Circulation*, *120*(16), 1640–1645.

# 1 Inhibiting the Absorption of Dietary Carbohydrates and Fats with Natural Products

Insulin resistance in metabolic syndrome results, at least, from the overconsumption of dietary carbohydrates, cholesterol, and triglycerides leading to the formation of visceral adiposity, increased plasma-free fatty acids, and secretion of pro-inflammatory cytokines, which at cellular level decrease insulin receptor functionality also known as insulin resistance.[1,2] Once insulin resistance is established, increased postprandial glycemia, according to genetic susceptibility, introduces the development of type 2 diabetes and cardiovascular insults.[3–6] Thus, inhibiting the absorption of dietary carbohydrates and fats (cholesterol and triglycerides) with natural products or extracts of medicinal plants constitutes one therapeutic strategy to prevent or manage insulin resistance in metabolic syndrome.

## 1.1 *Saururus chinensis* (Lour.) Baill.

*Synonyms*: *Saururopsis chinensis* (Lour.) Turcz.; *Saururopsis cumingii* C. DC.; *Saururus cernuus* Thunb.; *Saururus cumingii* C. DC.; *Saururus loureiri* Decne.; *Spathium chinense* Lour.

*Common name*: san bai cao (Chinese)

Subclass Magnoliidae, Superorder Piperanae, Order Piperales, Family Saururaceae

*Medicinal use*: wounds (Cambodia)

The hydrolysis of dietary triglycerides into glycerol and fatty acids is catalyzed by lingual, gastric, and pancreatic lipases.[7] There is a massive bulk of experimental evidence to demonstrate that extracts of medicinal plants in Asia, and most often polar extracts including aqueous, ethanol, and methanol, extracts have the ability to inhibit *in vitro* the enzymatic activity of lipase. For instance, ethanol extracts of *Saururus chinensis* (Lour.) Baill. (Figure 1.1) inhibited the enzymatic activity of pancreatic lipase with $IC_{50}$ equal to 81 μg/mL.[8] Oral administration of aqueous extract of this plant to rats on high-fat diet evoked a decrease in plasma triglycerides and an increase in fecal triglycerides, which suggests inhibition of triglyceride intestinal absorption.[9]

**FIGURE 1.1** *Saururus chinensis* (Lour.) Baill.

## 1.2 *Piper longum* L.

*Synonym*: *Chavica roxburghii* Miq.
*Common names*: bi ba (Chinese); long pepper
Subclass Magnoliidae, Superorder Piperanae, Order Piperales, Family Piperaceae
*Medicinal use*: facilitates digestion (China)
*History*: The plant was known to Hippocrates, Greek physician (circa 460–370 BC)

The main dietary carbohydrate is starch from plants that consists of amylose and amylopectin composed of linear chains glucose joined by α-1,4-glycosidic linkages, which are, especially for the later, branched by α-1,6-linkages.[10] Decrease in plasma glucose may be produced by decreased intestinal absorption of starch, and flavones in medicinal plants have the ability to hamper the enzymatic decomposition of starch and starch-derived products and sucrose. Apigenin-7,4'-dimethyl ether (Figure 1.2) isolated from the fruits of *Piper longum* L. Figure 1.2 inhibited α-amylase

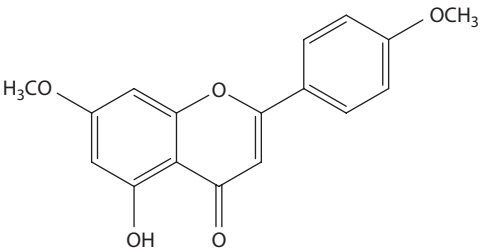



**FIGURE 1.2** Apigenin-7,4'-dimethyl ether.

*in vitro* with $IC_{50}$ value 98.1 μg/mL.[11] Acarbose used in therapeutic strategies to decrease postprandial hyperglycemia inhibited α-amylase with $IC_{50}$ 45.2 μg/mL.[11]

## 1.3 *Nelumbo nucifera* Gaertn.

*Synonyms*: *Nelumbium nuciferum* Gaertn.; *Nelumbo speciosa* Willd.; *Nymphaea nelumbo* L.
*Common names*: lian (Chinese); sacred lotus (English)
Subclass Ranunculidae, Superorder Proteanae, Order Nelumbonales, Family Nelumbonaceae
*Medicinal use*: anxiety (China)

Pancreatic α-amylase hydrolyzes starch α-1,4-linkages to yield maltose, maltotriose, and α-limit dextrin and vast body of pharmacological evidence suggest that flavonoids in medicinal plants account for the inhibition of pancreatic α-amylase.[12] For instance, ethanolic extract from leaves of *Nelumbo nucifera* Gaertn. inhibited the enzymatic activity of α-amylase and lipase with $IC_{50}$ values equal to 0.8 and 0.4 mg/mL, respectively *in vitro*.[13] The flavonoids quercetin 3-*O*-alpha-arabinopyranosyl-(1→2)-β-galactopyranoside, rutin, catechin, hyperoside, isoquercitrin, quercetin, astragalin, hyperin, kaempferol, and myricetin present in this plant may account for these effects.[14] Myricetin (Figure 1.3) inhibited α-amylase activity with an $IC_{50}$ value of 30.2 μM.[15] Liu et al. (2013) reported the ability of a total flavonoid fraction of leaves of *Nelumbo nucifera* Gaertn. to inhibit yeast α-amylase, yeast α-glucosidase, and porcine lipase with $IC_{50}$ values of 2.2, 1.8, and 0.3 mg/mL, respectively.[16] In this experiment, acarbose used as positive standard inhibited yeast α-amylase and α-glucosidase with $IC_{50}$ values of 0.4 and 0.6 mg/mL, respectively.[16] Quercetin-3-*O*-β-D-arabinopyranosyl-(1→2)-β-D-galactopyranoside and quercetin-3-*O*-β-D-glucuronide (Figure 1.4) isolated from this plant inhibited porcine pancreatic lipase with $IC_{50}$ values of 52.9 and 17.1 μg/mL, respectively.[17] Total flavonoid fraction of leaves of this aquatic plant given orally at a dose of 240 mg/kg/day to Wistar rats, which are often used for metabolic studies, on high-fat diet for 2 weeks decreased plasma triglycerides from 2.5 to 1.2 mmol/L.[16] The leaves

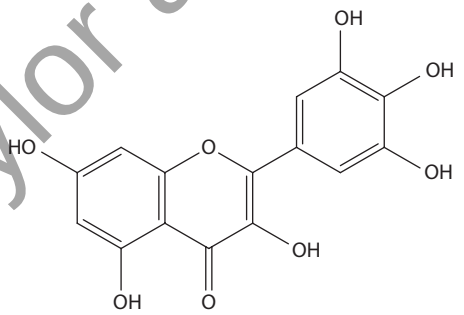



**FIGURE 1.3** Myricetin.

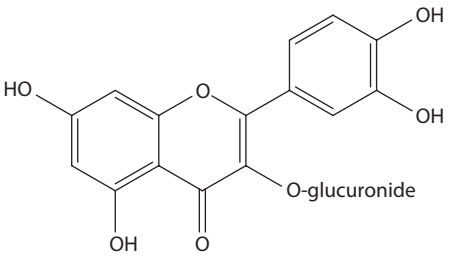



**FIGURE 1.4** Quercetin-3-*O*-β-D-glucuronide.

of *Nelumbo nucifera* Gaertn. contain the isoquinoline alkaloids (6*R*,6aR)-roemoerine-$N_{\beta}$-oxide, liriodenine, pronuciferine, oleracein E as well as the phenolics trans-*N*-coumaroyltyramine, cis-*N*-coumaroyltyramine, trans-*N*-feruloyltyramine, cis-*N*-feruloyltyramine, which inhibited the enzymatic activity of pancreatic lipase *in vitro* (ii).[18] Being able to inhibit the absorption of carbohydrates and triglycerides, the leaves of this astringent medicinal plant, if not toxic, could be conceptually seen as a dietetic material of interest for metabolic syndrome. Clinical studies in this direction are warranted.

## 1.4 *Coptis chinensis* Franch.

*Common name*: huang lian (Chinese)
Subclass Ranunculidae, Superorder Ranunculanae, Order Ranunculales, Family Ranunculaceae
*Medicinal use*: fever (China)

As a consequence of insulin resistance, postprandial glycaemia in metabolic syndrome is elevated and high concentration of circulating glucose that could be referred to a state of "*glucotoxicity*" contribute to the development of type 2 diabetes, cardiovascular diseases, and all that cause mortality.[19] *Coptis chinensis* Franch. (Figure 1.5) elaborates the alkaloid berberine which when given orally at a

**FIGURE 1.5** *Coptis chinensis* Franch.

dose of 200 mg/kg once daily reduced the glycemia of diabetic rodents and inhibited the enzymatic activity of sucrase and maltase.[20] In a clinical study involving type 2 diabetes outpatients, the intake of 500 mg of berberine 3 times daily evoked a reduction in blood glucose.[21] Thus, being relatively nontoxic, and poorly absorbed, berberine could conceptually be seen as a potential agent to mitigate glucose absorption in metabolic syndrome.

## 1.5 *Tinospora crispa* (L.) Hook. f. & Thomson

*Synonyms*: *Menispermum crispum* L.; *Tinospora gibbericaulis* Hand.-Mazz.; *Tinospora mastersii* Diels; *Tinospora rumphii* Boerl.; *Tinospora thorelii* Gagnep.
*Common names*: bo ye qing niu dan (Chinese); akar putarwali (Malay); makabuhay (Philippines); boraphet (Thai)
Subclass Ranunculidae, Superorder Ranunculanae, Order Menispermales, Family Menispermaceae
*Medicinal use*: jaundice (Vietnam)

Degradation products of starch are hydrolyzed in the jejunum into free absorbable glucose by 4 brush border α-glucosidases arranged into 2 enzymatic complexes termed as sucrase–isomaltase and maltase–glucoamylase.[22] Members of the family Menispermaceae often accumulate isoquinoline alkaloids that hamper glucose absorption by inhibiting enterocyte membrane bound α-glucosidases. As an example, *Tinospora crispa* (L.) Hook. f. & Thomson synthetize palmatine, jatrorrhizine, and magnoflorine that inhibited the enzymatic activity of sucrase with $IC_{50}$ of 36.2, 23.4, and 9.8 μg/mL, respectively.[23] In the same experiment, palmatine, jatrorrhizine, and magnoflorine inhibited the enzymatic activity of maltase with $IC_{50}$ values equal to 22, 38.4, and 7.6 μg/mL.[23] Magnoflorine at a dose of 20 mg/kg mitigated the raise in glycaemia induced by oral administration of 2 g/kg of glucose to rodents.[23] Magnoflorine is known to induce hypotension when parenterally administered and to be nontoxic in animals when given orally.[24]

## 1.6 *Nigella sativa* L.

*Common names*: Krishna jiraka (India); habbatus sauda (Malay); fennel flower seeds
Subclass Ranunculidae, Superorder Ranunculanae, Order Menispermales, Family Ranunculaceae
*Medicinal use*: in Malaysia, the seeds are ingested to invigorate
*History*: Known of Hippocrates Greek physician (circa 460–370 BC) as tonic spice

Glucose released from maltose, maltotriose, dextrin, and sucrose, it is actively engulfed in jejunal brush border by integral sodium-dependent glucose transporter-1 (SGLT-1) located in the apical cytoplasmic membrane of enterocytes.[25] *Nigella sativa* L. contains natural product(s), yet to be identified, with the ability to attenuate intestinal glucose absorption by inhibiting enterocytes integral membrane $Na^+$-glucose transporter 1 (SGLT1).[26] Aqueous extract from seeds of *Nigella sativa* L. given orally for 6 weeks to Sprague–Dawley rats at a dose of 0.2 g/kg/day improved glycaemia as well as body weight as efficiently as metformin at a dose of 300 mg/kg/day.[26] *In vitro*, this extract at a dose of 1 ng/mL prophylactically inhibited glucose intake by sodium-dependent glucose transporter-1 (SGLT-1) of isolated jejunal mucosa by 81.8%.[26] Besides, methanol extract from seeds of *Nigella sativa* L. at a concentration of 2.5 mg/mL completely inhibited porcine pancreatic lipase *in vitro*.[27] Being relatively nontoxic, consumption of seeds of *Nigella sativa* L. may limit glucose and fatty acids absorption in

metabolic syndrome. Like most medicinal plants used since time immemorial, and with the disappearance of pharmacognosy and herbalism from what we call today *Schools of Pharmacy* (?), the exact dose of these seeds to be taken seems unknown.

## 1.7 *Celosia argentea* L.

*Synonym*: *Celosia cristata* L.
*Common names*: qing xiang (Chinese); barhichuda (India); bayam (Malay); palonpalongan (Philippines); wild cockscomb
Subclass Caryophyllidae, Superorder Caryophyllanae, Order Caryophyllales, Family Amaranthaceae
*Medicinal use*: dysentery (Malaysia)

Evidence supports the view that medicinal plants in the family Amaranthaceae Juss. inhibit the enzymes of carbohydrate intestinal absorption on account of their triterpenoid saponins. On such medicinal plant is *Celosia argentea* L., an ethanolic extract of which inhibited porcine pancreatic amylase and yeast α-glucosidase *in vitro* with $IC_{50}$ values of 1.6 and 1 mg/mL, respectively (acarbose: 0.1 and 0.9 mg/mL, respectively).[28,29]

## 1.8 *Kochia scoparia* (L.) Schrad.

*Synonym*: *Chenopodium scoparium* L.
*Common names*: ti fu (Chinese); fire weed
Subclass Caryophyllidae, Superorder Caryophyllanae, Order Caryophyllales, Family Chenopodiaceae
*Medicinal use*: promote urinations (China)

In the stomach, dietary triglycerides and cholesteryl esters are dispersed in coarse oil globules, which are emulsified by bile acids in the duodenum into small droplets.[30] Pancreatic cholesteryl ester esterase and lipase catalyse the hydrolysis of cholesteryl ester and triglycerides to form mixed micelles which are then absorbed by the apical cytoplasmic membrane of brush border enterocytes.[30] Saponins, which are abundant in members of the family Amaranthaceae Juss., are amphiphilic and disrupt the formation of mixed micelles and subsequent absorption of fatty acids and cholesterol by enterocytes.[31] Ethanol extract from fruits of *Kochia scoparia* (L.) Schrad. (Figure 1.6) at concentration of 2 mg/mL inhibited the enzymatic activity of lipase *in vitro* by 50%. The extract given orally once at a dose of 250 mg/kg to rats abrogated plasma triglycerides 2 hours peak after oral administration of a lipid emulsion.[32] Mice fed with high-fat diet with 3% of this extract emitted high triglycerides in their feces providing evidence of nonabsorption of dietary triglyceides.[32] The same regimen prolonged for 9 weeks brought body weights close to those observed for rodents fed with normal diet.[2] Further, treated mice, compared to untreated group, had a reduction in parametrial adipose tissue mass from 1.8 to 1.2 g and a reduction of hepatic total cholesterol from 12.9 to 7.4 μmol/L.[32] Vinarova et al. (2015) studied the effects of various saponins on the cholesterol bioaccessibility from emulsions stabilized by Tween 80 and found that saponins decrease cholesterol bioaccessibility by displacing cholesterol from mixed micelles.[30] These findings raise the question whether the intake of saponin containing Asian medicinal plants could effectively decrease the absorption of triglycerides and cholesterol and prevent or manage metabolic syndrome.

**FIGURE 1.6** *Kochia scoparia* (L.) Schrad.

## 1.9 *Rheum ribes* L.

*Common name*: warted-leaved rhubarb
Subclass Caryophyllidae, Superorder Polygonanae, Order Polygonales, Family Polygonaceae
*Nutritional use*: food (Turkey)
*History*: The plant was known to Serapion (twelfth century), Arabic physician as astringent and cold and prescribed for the treatment of cholera and hemorrhoids

Aqueous liquid extract from roots of *Rheum ribes* L. (10g/100 mL) a concentration of 50 mg/mL halved glucose liberation from starch by α-amylase by 50%.[33] At a dose of 125 mg/kg, this extract decreased peak glycaemia at 45 minutes in oral starch tolerance test similar to 3 mg/kg of acarbose in Sprague–Dawley rats at 5 mM.[33] The petioles of members of the genus *Rheum* are particularly rich in fibers, and it must be recalled that dietary fiber adsorb bile acids and cholesteryl ester and promote bile formation and cholesterol fecal excression. Such fibers are particularly present in the leaf stalks of *Rheum officinale* Baill., which given at a dose of 27 g/day to hypercholesterolaemic volunteers for 4 weeks following habitual diets had no effect on the body mass index but induced a mild decrease of total cholesterol and triglycerides from 2.1 to 1.8 mmol/L.[34]

## 1.10 *Camellia sinensis* (L.) Kuntze

*Synonym*: *Thea chinesis* L.
*Common names*: cha (Chinese); tea
Subclass Dillenidae, Superorder Ericanae, Order Theales, Family Theaeae
*Medicinal use*: tonic (China)
*History*: Used since time immemorial in China and listed in the penst'sao kang mu

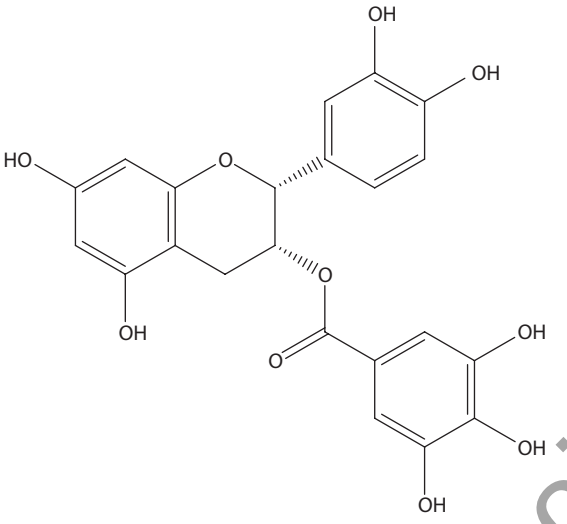



**FIGURE 1.7** (−)-Epigallocatechin-3-gallate.

Evidence suggests beneficial effect of green tea catechins on metabolic syndrome (partly on account of lipase, α-amylase, and α-glucosidase inhibition).[35] Wild mice and rats, contrary to human, do not spontaneously develop metabolic syndrome. C57BL/6J mice are used to assess the metabolic effects of medicinal plants because these genetically engineered rodents on high-fat diet develop obesity, hyperlipidemia, hyperinsulinemia, hyperglycemia, insulin resistance, and glucose intolerance.[36] C57BL/6J mice on high-fat diet had a 5.4% weight reduction following the inclusion of 0.3% of green tea (−)-epigallocatechin-3-gallate in diet for 7 weeks.[37] This regimen increased by 29.4% fecal triglycerides as a result of pancreatic lipase inhibition.[37] (−)-Epigallocatechin-3-gallate (Figure 1.7) inhibited *in vitro* the enzymatic activity of pancreatic lipase with an $IC_{50}$ value equal to 7.5 μmol/L.[37] Fei et al. (2014) provided evidence that phenolic fraction of *Camellia sinensis* (L.) Kuntze could inhibit the enzymatic activity of pancreatic α-amylase *in vitro* with an $IC_{50}$ of 0.3 μg/mL.[38] From this fraction, (−)-epigallocatechin gallate and (−)-epigallocatechin 3-*O*-(3-*O*-methyl) gallate inhibited the enzymatic activity of pancreatic α-amylase with an $IC_{50}$ of 0.3 and 0.5 μg/mL, respectively.[38] Green tea or the unfermented leaves of *Camellia sinensis* (L.) Kuntze is consumed daily in Asia and should be recommended, at normal dose, in metabolic syndrome.

## 1.11 *Garcinia mangostana* L.

*Synonym*: *Mangostana garcinia* Gaertn.
*Common names*: mangustan (Malay); mangosteen
Subclass Dillenidae, Superorder Ericanae, Order Hypericales, Family Clusiaceae
*Medicinal use*: diarrhoea (Malaysia)
*History*: By the year 1880, the husk of fruits of *Garcinia mangostana* L. was exported from Malaysia as a reputed astringent remedy to treat diarrhea

In the jejunum, sucrase–isomaltase hydrolyses α-1,4-linkages of maltose and sucrose and maltase–glucoamylase hydrolyses α-1,4-linkages of maltose, maltotriose, and limited dextrins.[22] Evidence suggests that prenylated xanthones elaborated by members of the family Clusiaceae have the ability to inhibit α-glucosidases. Ethanol extract from fruit rinds of *Garcinia mangostana* L. inhibited of α-glucosidase with an $IC_{50}$ value of 3.2 μg/mL.[39] This extract given orally and prophylactically at a single dose of 100 mg/kg to streptozotocin-induced diabetic Sprague–Dawley rats reduced glycaemia by 40% during maltose oral challenge.[39] From this extract, the prenylated xanthones

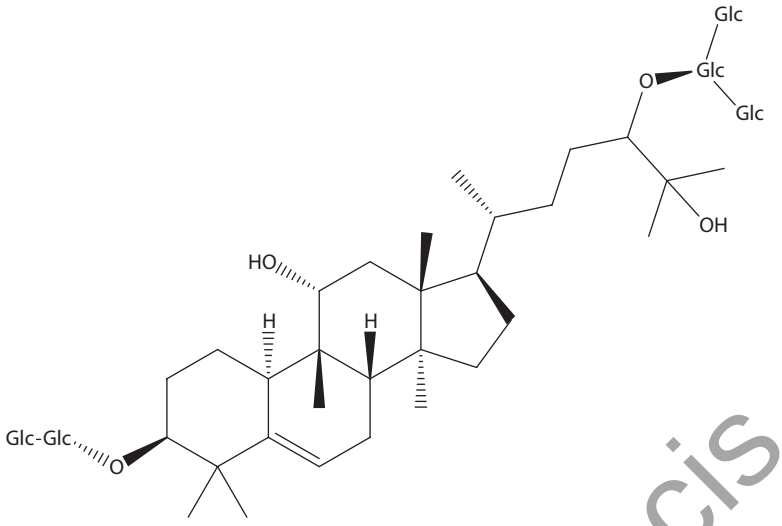



**FIGURE 1.8** γ-Mangostin.

β-mangostin, allanxanthone E, α-mangostin, mangostingone, γ-mangostin (Figure 1.8), gartanin, and smeaxanthone A inhibited the enzymatic activity of α-glucosidase with $IC_{50}$ values below 40 μM, respectively.[39]

## 1.12 *Barringtonia racemosa* (L.) Spreng.

Subclass Dillenidae, Superorder Ericanae, Order Lecythidales, Family Lecythidaceae
*Medicinal use*: rheumatism (Philippines)

α-Glucosidases are inhibited by oleanane and lupane triterpenes that occur in members of the family Lecythidaceae such as *Barringtonia racemosa* (L.) Spreng.[40] Defatted methanol extract from fruits of *Barringtonia racemosa* (L.) Spreng inhibited α-glucosidase activity with an $IC_{50}$ equal to 26.9 μg/mL. From this extract, the polyhydroxy oleanane triterpenes racemosol C and D isolated inhibited α-glucosidase with $IC_{50}$ values of 5.6 and 45.3 μM, respectively.[41] In the same experiment, the triterpene betulinic acid (Figure 1.9) inhibited α-glucosidase with an $IC_{50}$ value equal to 7.8 μM. 3β-acetoxy-16β-hydroxybetulinic acid, isolated from another plant, inhibited α-glucosidase with an $IC_{50}$

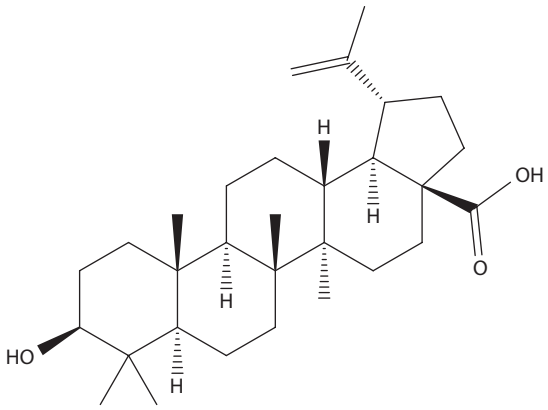



**FIGURE 1.9** Betulinic acid.

value equal to 7.6 μM implying that the triterpene backbone is sufficient for activity.[42] Comparatively, acarbose inhibited the enzymatic activity of yeast α-glucosidase with $IC_{50}$ value of 780 μM.[40]

## 1.13 *Embelia ribes* Burm.f.

*Common names*: bai hua suan teng guo (Chinese); vidanga (India)
Subclass Dilleniidae, Superorder Primulanae, Order Primulales, Family Myrsinaceae
*Medicinal use*: jaundice (India)
*History*: *Embelia ribes* Burm.f. was known of Sushruta (circa 600 BC) an Ayurvedic physician, notably to expel intestinal worms

α-Glucosidases can be inhibited *in vitro* by various types of phenolic compounds explaining the observation that ethanol, aqueous, or methanol extracts of medicinal plants inhibit this group of enzymes as a result of a synergistic effect. *Embelia ribes* Burm.f. elaborates in its leaves the flavonoids kaempferol and quercitrin, and the lignans (+)-syringaresinol-β-D-glucoside, and (+)-syringaresinol that inhibited yeast α-glucosidase with $IC_{50}$ below 90 μM, respectively (acarbose: $IC_{50}$ of 214.5 μM).[43] From the stems, embeliphenol A, 5-(8'Z-heptadecenyl)-resorcinol, 1-(3,5-dihydrophenyl)nonan-1-one, 3-methoxyl-5-pentylphenol (Figure 1.10), and eupomatenoid-8 inhibited yeast α-glucosidase with $IC_{50}$ of 47.4, 41.2, 10.4, 66.9, and 65.7 μM, respectively (acarbose: $IC_{50}$ of 214.5 μM).[44] The antidiabetic use of the plant could be, at least partly, due to α-glucosidase inhibition.

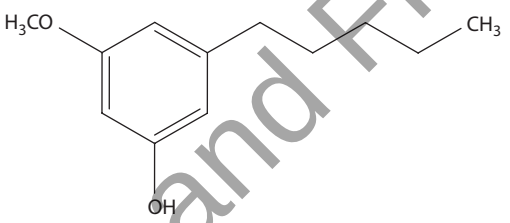



**FIGURE 1.10** 3-Methoxyl-5-pentylphenol.

## 1.14 *Gynostemma pentaphyllum* Makino

*Common name*: jiao gu lan (Chinese)
Subclass Dilleniidae, Superorder Violanae, Order Cucurbitales, Family Cucurbitaceae
*Medicinal use*: tonic (China)
*Pharmacological target*: atherogenic hyperlipidemia

Orlistat is a specific and potent pancreatic lipase inhibitor derived from lipstatin, a β-lactone isolated from *Streptomyces toxytricini* used in therapeutic to reduce triglyceride absorption in obese patients.[45,46] However, orlistat offers about 30% efficacy and is responsible for gastro-intestinal, nervous, endocrine, and renal system side effects, justifying the development of safer, natural pancreatic lipase inhibitor.[46] Extract of *Gynostemma pentaphyllum* Makino (containing more than 90% of saponins termed gypenosides) given orally to obese Zucker fatty rats at a dose of 250 mg/kg/day for 3 weeks and administered 1 hour before oral olive oil administration decreased postprandial triglyceridemia by 18% after 5 hours, suggesting pancreatic lipase inhibition.[47] This extract given to Sprague–Dawley at a concentration of 125 mg/kg concomitantly with oral loading of sucrose had no effect of postprandial glycemia but inhibited yeast α-glucosidase activity *in vitro* with an $IC_{50}$ value of 42.8 μg/mL (acarbose: 53.9 μg/mL).[47] That result suggests that inhibition of yeast α-glucosidase *in vitro* by saponins is not correlated with *in vivo* with intestinal α-glucosidase because triterpene glycosides are metabolized by bacteria in the guts. In a subsequent study, gypenosides from

*Gynostemma pentaphyllum* Makino given orally for 5 weeks at a dose of 200 mg/kg/day to Wistar rats fed with high-fat diet reduced plasma cholesterol and triglycerides to about 40% and 60%.[48] These dammarane saponins normalized hepatic cholesterol and hepatic triglycerides as efficiently as simvastatin at a dose of 10 mg/kg/day and halved the enzymatic activity of 3-hydroxy-3-methylglutaryl-coenzyme A reductase.[48] This protein is a rate limiting enzyme in the synthesis of cholesterol.[49] Su et al. (2016) made the demonstration that gypenosides from *Gynostemma pentaphyllum* Makino at a concentration of 0.2 mg/mL inhibited porcine pancreatic lipase activity to about 40%, whereas orlistat evoked the same concentration approximately 95% inhibition.[50] These saponins did not bind to the catalytic pocket of lipases but instead inhibited cholesterol in mixed micelles via increase in size of mixed micelles.[50] It must be recalled that obese Zucker fatty rats are genetic model of metabolic syndrome due to mutated leptin receptor developing hypercholesterolaemia, hypertriglyceridemia, adipocyte hyperplasia, obesity, hyperglycemia, hyperinsulinemia, and glucose intolerance.[51] *Gynostemma pentaphyllum* Makino's ability to prevent triglyceride and cholesterol absorption in obese Zucker fatty rats by compromising mixed micelle formation and lipase inhibition could conceptually be of value to prevent hypercholesterolemia and hypertriglycemia in metabolic syndrome. Clinical trials are warranted.

## 1.15 *Lagenaria siceraria* (Mol.) Standl.

*Synonyms*: *Cucumis mairei* H. Lév.; *Cucurbita lagenaria* L.; *Cucurbita leucantha* Duchesne; *Cucurbita siceraria* Molina; *Lagenaria vulgaris* Ser.
*Common names*: hu lu (Chinese); kalubay (Philippines); bottle gourd
Subclass Dilleniidae, Superorder Violanae, Order Cucurbitales, Family Cucurbitaceae
*Medicinal use*: cough (Philippines)

Plant sterols also known as phytosterols, because of their hydrophobicity and high affinity for mixed micelles in the small intestine, displace cholesterol at intestinal micelles levels and inhibit cholesterol absorption resulting in it fecal excression.[52,53] Medicinal plants in the family Cucurbitaceae produce phytosterol and for instance, a mixture of fucosterol, stigmasterol, and stigmasta 7,22-dien-3β,4β-diol isolated from *Lagenaria siceraria* (Molina) Standl. given orally to hyperlipidemic Wistar rats at a dose of 30 mg/kg/day for 30 days decreased cholesterol and triglycerides from 269 to 146.6 mg/dL and from 175.5 to 136.6 mg/dL, respectively.[54]

## 1.16 *Siraitia grosvenorii* (Swingle) C. Jeffrey ex A.M. Lu & Z.Y. Zhang

*Synonyms*: *Momordica grosvenorii* Swingle; *Thladiantha grosvenorii* (Swingle) C. Jeffrey
*Common name*: luo han guo (Chinese)
Subclass Dilleniidae, Superorder Violanae, Order Cucurbitales, Family Cucurbitaceae
*Medicinal use*: bronchitis (China)

Delaying intestinal glucose absorption is an important therapeutic strategy to fight metabolic syndrome because it decreases postprandial glycemia, decreases insulin resistance, evokes mild loss of body weight, and improves serum lipid profiles.[55] Aqueous extract from fruits of *Siraitia grosvenorii* (Swingle) C. Jeffrey ex A.M. Lu & Z.Y. Zhang given intragastrically and prophylactically to Wistar rats at a single dose of 0.1 g/kg decreased postprandial glycaemia when administered with oral load of maltose.[56] From this extract, a mixture of triterpene glycosides at a dose of 0.1 g/kg decreased maltose-induced, postprandial glycaemia to 70% after 30 minutes.[56] This fraction inhibited *in vitro* the enzymatic activity of rat intestinal maltase with an $IC_{50}$ value equal to 5 mg/mL.[56] From this fraction, the triterpene saponins mogroside V. (Figure 1.11) inhibited rat-intestinal maltase *in vitro* with an $IC_{50}$ of 18 mg/mL.[56] It should be noted that peak blood glucose values in rats are obtained much earlier (15–45 minutes) than in human subjects (around 60 minutes).[57] Being nontoxic, the fruits of

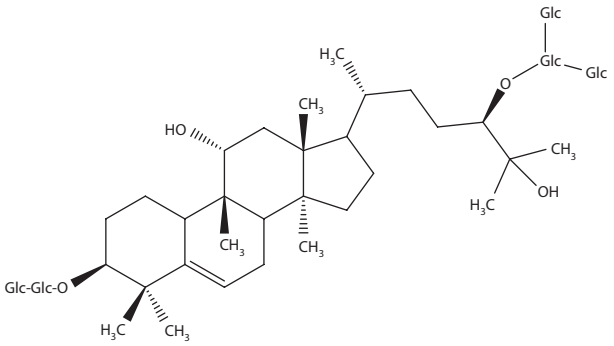



**FIGURE 1.11** Mogroside V.

*Siraitia grosvenorii* (Swingle) C. Jeffrey ex A.M. Lu & Z.Y. Zhang could, be incorporated in the diet of subjects with metabolic syndrome. Clinical studies in this direction are needed.

## 1.17 *Brassica oleracea* L.

*Synonyms*: *Crucifera brassica* E.H.L. Krause; *Napus oleracea* (L.) K.F. Schimp. & Spenn.
*Common names*: ye gan lan (Chinese); cabbage
Subclass Dilleniidae, Superorder Capparanae, Order Capparales, Family Brassicaceae
*Medicinal use*: carminative (China)

Anthocyanin-rich extract of *Brassica oleracea* L. (Figure 1.12) given orally to Charles Foster rats for 8 weeks at a dose of 100 mg/kg/day reduced plasma cholesterol from 216.7 to 92.1 mg/dL and

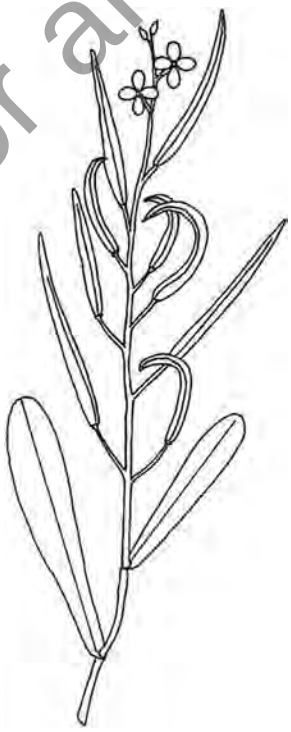


**FIGURE 1.12** *Brassica oleracea* L.

triglycerides from 90.5 to 69.6 mg/dL, low density lipoproteins from 230.8 to 67.3 mg/dL, and very low-density lipoproteins from 18.1 to 13.2 mg/dL.[58] This treatment increased triglyceride faeces from 5 to 12.3 mg/g, increased faeces cholesterol from 5.4 to 9 mg/g, and boosted the fecal excression of cholic acid and deoxycholic acid implying the inhibition of cholesterol and triglycerides intestinal absorption.[58]

## 1.18 *Cotylelobium melanoxylon* (Hook. f.) Pierre

*Synonym*: *Anisoptera melanoxylon* Hook. f.
*Common names*: resak bukit (Indonesia); khiam (Thailand)
Subclass Dillenidae, Superorder Malvanae, Order Malvales, Family Dipterocarpaceae
*Medicinal use*: diabetes (Indonesia)

In type 2 diabetic patients the activity of sucrase–isomaltase is abnormally high.[59] Oligostilbenes have the ability to inhibit α-glucosidase *in vitro* and *in vivo*. These phenolic natural products are accumulated in members of the family Dipterocarpaceae. One such oligostilbene is vaticanol G which at a single oral dose of 50 mg/kg administered 30 minutes before oral loading of sucrose decreased postprandial glycemia of rats from 188.3 to 127.2 mg/dL at 30 minutes, suggesting α-glucosidase inhibition (acarbose 10 mg/kg: 114.8 mg/mL).[60] From the same plant, vaticanol A and E at a single dose of 50 mg/kg administered 30 minutes before oral loading of sucrose decreased the postprandial glycemia from 188.3 to 147.3 mg/dL and from 188.3 to 156.8 mg/dL at 30 minutes, respectively (acarbose 10 mg/kg: 114.8 mg/mL).[60] Further, vaticanol A at a single oral dose of 200 mg/kg lowered plasma triglycerides from 535.6 to 368.6 mg/dL, 2 hours after olive-oil loading in ddY mice indicating pancreatic lipase inhibition (orlistat at 20 mg/kg: 198.6 mg/dL).[60] Vaticanol E at a single oral dose of 200 mg/kg decreased plasma triglycerides from 535.6 to 326.3 mg/dL, 2 hours after olive-oil loading in male ddY mice (orlistat at 20 mg/kg: 198.6 mg/dL).[60] Vaticanol G at a single oral dose of 200 mg/kg decreased plasma triglycerides from 535.6 to 245.7 mg/dL 2 hours after olive-oil loading in male ddY mice.[60] *In vitro*, vaticanol A inhibited the enzymatic activity of maltase, sucrase, and lipase with $IC_{50}$ values of 218, 148, and 52 μM, respectively (acarbose: 2 and 1.7 μM orlistat: 0.05 μM).[60] *In vitro*, vaticanol E inhibited the enzymatic activity of maltase, sucrase, and lipase with $IC_{50}$ values of 342, 89, and 86 μM.[60] *In vitro*, vaticanol E inhibited the enzymatic activity of maltase, sucrase with $IC_{50}$ superior to 400 μM and inhibited lipase with $IC_{50}$ values of and 59 μM.[60]

## 1.19 *Shorea roxburghii* G. Don

*Common names*: jalari (India); Meranti temak nipis (Malay); phayom (Thai); Talooralac tree
Subclass Dilleniidae, Superorder Malvanae, Order Malvales, Family Diperocarpaceae
*Medicinal use*: diarrhoea (Thailand)

Methanol extract from barks of *Shorea roxburghii* G. Don given orally at a single dose of 250 mg/kg to rodents decreased postprandial glycaemia 30 minutes after sucrose loading from 229.9 to 207.6 mg/dL.[61] From this extract, hemsleyanol D, (+)-α-viniferin and (−)-balanocarpol at a dose of 200 mg/kg reduced, in the same experiment, glycaemia from 232.9 to 142.4, 153.5, and 169.2 mg/dL, respectively.[61] *In vitro*, hemsleyanol D and (+)-α-viniferin inhibited the enzymatic activity of maltase with $IC_{50}$ values equal to 266 and 172 μM and sucrase with $IC_{50}$ values equal to 218 and 234 μM, respectively.[61] In regards to lipase, methanol extract from bark of *Shorea roxburghii* G. Don inhibited the enzymatic activity of lipase with an $IC_{50}$ value equal to 31.6 μg/mL. From this extract, phayomphenol A2, (−)-hopeaphenol, (+)-isohopeaphenol, hemsleyanol D, (+)-α-viniferin, and (−)-balanocarpol administered orally to fasted ddY mice 30 minutes prior to olive-oil intake decreased plasma triglycerides from 546.7 to 217.5, 269.5, 237.2, 274.6, 266.9, and 240.5 mg/dL, respectively, whereas orlistat reduced triglyceridaemia to 203.8 mg/dL.[62] *In vitro*, (−)-hopeaphenol, (+)-isohopeaphenol, hemsleyanol D, (+)-α-viniferin inhibited the enzymatic activity with $IC_{50}$ values below 50 μM, whereby (−)-balanocarpol was inactive and orlistat had an $IC_{50}$ value equal 0.05 μM.[62]

## 1.20 *Broussonetia kazinoki* Siebold & Zucc.

*Synonym*: *Broussonetia monoica* Hance
*Common name*: chu (Chinese)
Subclass Dilleniade, Superorder Malvanae, Order Urticales, Family Moraceae
*Medicinal use*: aphrodisiac (Korea)

The stem bark of *Broussonetia kazinoki* Siebold & Zucc. shelter the diphenylpropanes broussonone A (Figure 1.13) broussonin A and B, the flavans 7,4'-dihydroxyflavan and 3',7-dihydroxy-4'-methoxyflavan, which at a concentration of 100 μM inhibited the enzymatic activity of pancreatic lipase by 71.9%, 50.7%, 40.4%, 55.6%, and 24.8%, respectively, whereas orlistat at 1 μM evoked 60.4% inhibition.[63]

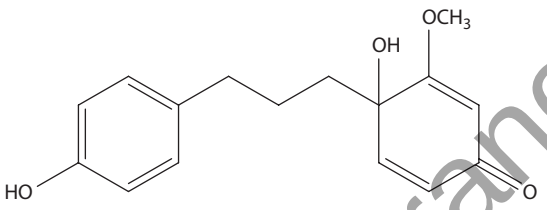
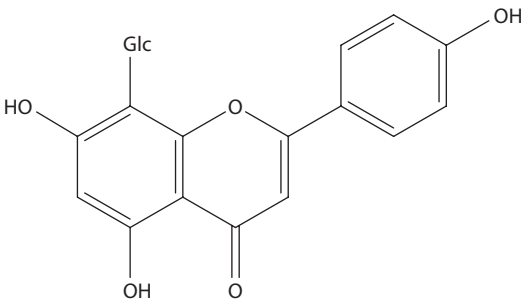



**FIGURE 1.13** Broussonone A.

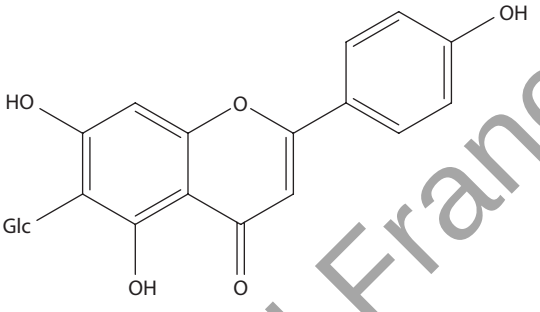
## 1.21 *Ficus deltoidea* Jack

*Synonyms*: *Ficus diversifolia* Blume; *Ficus ovoidea* Jack
*Common names*: ara burong (Malay); Mistletoe Fig
Subclass Dillenidae, Superorder Malvanae, Order Urticales, Family Moraceae
*Medicinal use*: diabetes (Malaysia)

In man, throughout a 24-hour period, arterial plasma glucose average approximatively 90 mg/dL.[64] Physiologically, the consumption of 75 g of glucose evokes, after 2 hours, a rise in plasmatic glucose concentration that remains below 140 mg/dL (7.8 mmol/L).[64,65] In obese patients, a 2-hour post oral 75 g glucose intake glycemia ranging from 7.8 mmol/L (140 mg/dL) to 11.1 mmol/L (200 mg/dL) evidences a state of impaired glucose tolerance as defined by the World Health Organization (2006). In diabetic patients, 2-hour plasma glucose is equal to or superior to 200 mg/dL (11.1 mmol/L).[65] In order to suppress postprandial hyperglycemia, a number of α-glucosidase inhibitors delaying the absorption of glucose from dietary carbohydrates have been developed including acarbose, miglitol, and voglibose, which have unpleasant side effects.[66] The flavones C-glycosides vitexin and isovitexin (Figure 1.14) isolated from *Ficus deltoidea* Jack given orally at a dose of 100 mg/kg decreased 30 minutes postprandial glycemia in normal mice or diabetic rats loaded with sucrose via α-glucosidase inhibition.[67] In a subsequent study, Yang et al. (2014) provided evidence that vitexin and isovitexin inhibited α-amylase activity with Ki values of 569.6 and 75.8 μg/mL, respectively.[68] The antidiabetic activity of *Ficus deltoidea* Jack could at least be imparted via inhibition of glucose absorption from dietary carbohydrates. The toxicity of the plant appears to be unknown and preclinical studies are needed.




Vitexin




Isovitexin

**FIGURE 1.14** Flavones C-glycosides from *Ficus deltoidea* Jack.

## 1.22 *Phyllanthus reticulatus* Poir.

*Synonyms*: *Glochidion microphyllum* Ridl.; *Phyllanthus dalbergioides* Wall. ex J.J. Sm.; *Phyllanthus erythrocarpus* Ridl.

*Common names*: xiao guo ye xia zhu (Chinese); kayu darah belut (Malay); matang bulud (Philippines)

Subclass Dillenidae, Superorder Euphorbianae, Order Euphorbiales, Family Phyllanthaceae

*Medicinal use*: sore throat (Malaysia)

Ethanol extract of leaves of *Phyllanthus reticulatus* Poir. given orally to alloxan-induced diabetic Swiss mice at dose of 1 g/kg decreased after 24 hours plasma glucose from 291.3 to 206.3 mg%.[69] Given daily for 21 days, this extract at dose of 1 g/kg decreased plasma glucose from 291.8 to 186 mg%, whereas untreated animals had a variation of glycaemia from 387 to 325 mg%.[69] The astringency of this plant is most probably owed to ellagitannins and gallic acid that may inhibit α-amylase and/or α-glucosidase.[70] Methyl gallate (Figure 1.15) inhibits α-glucosidase *in vitro*.[71] It is tempting to speculate that ellagitannins and their derivatives in *Phyllanthus reticulatus* Poir. could inhibit pancreatic lipase. Maruthappan and Shree reported that the intake of 500 mg/kg/day of aqueous extract from the plant to rats for 45 days on high-fat diet decreased plasma triglycerides.[72]

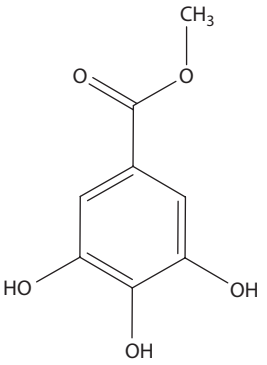



**FIGURE 1.15** Methyl gallate.

## 1.23 *Euphorbia thymifolia* L.

*Synonyms*: *Anisophyllum thymifolium* (L.) Haw.; *Chamaesyce thymifolia* (L.) Millsp.; *Euphorbia philippina* J. Gay ex Boiss.
*Common names*: qian gen cao (Chinese); Laghu dugdhi (India); Thyme-leaved Spurge
Subclass Dillenidae, Superorder Euphorbianae, Order Euphorbiales, Family Euphorbiaceae
*Medicinal use*: diabetes (Bangladesh)
*History*: The plant was known to Sushruta (600 BC) Ayurvedic physician

Methanol extract of *Euphorbia thymifolia* L. given orally to Swiss albino mice at a single dose of 400 mg/kg 1 hour before oral administration of glucose decreased glycaemia to 60.5%, whereas glibenclamide at 10 mg/kg evoked a 48.6% fall in glycemia.[73] Note that the plant accumulates ellagitannins and quercetin glycosides.[74,75,78,79] Ellagitannins in this plants may inhibit carbohydrate and triglycerides intestinal absorption through inhibition of α-amylase, α-glucosidase, and pancreatic lipase. However, decrease in postprandial glycemia during oral loading of glucose is by itself independent of α-amylase or α-glucosidase but may result from inhibition of glucose by enterocytes increased insulin secretion or increased uptake of glucose in skeletal muscles. Further pharmacological and toxicological studies on the benefits of *Euphorbia thymifolia* L. for metabolic syndrome are needed.

## 1.24 *Sinocrassula indica* (Decne.) A. Berger

*Synonyms*: *Crassula indica* Decne.; *Sedum indicum* (Decne.) Raym.-Hamet
*Common name*: shi lian (Chinese)
Subclass Rosidae, Superoder Rosanae, Order Saxifragales, Family Crassulaceae
*Medicinal use*: cough (India)

Methanol extract of *Sinocrassula indica* (Decne.) A. Berger (containing flavonoids including quercetin, luteolin, kaempferol) given orally to rats at a single dose of 500 mg/kg decreased postprandial glycaemia from 166.3 to 121.9 mg/dL at 30 minutes during oral sucrose challenge (tolbutamide: 25 mg/kg: 138.1 mg/dL).[76] The same regimen applied to rats challenged with oral glucose decreased glycaemia but had no activity against intraperitoneal glucose loading, indicating an activity elicited at intestinal level.[76] It must be noted that glucose released from maltose, maltotriose, dextrin, and sucrose is actively absorbed in brush border enterocytes by integral sodium-dependent glucose transporter-1 (SGLT-1) located in the apical cytoplasmic membrane.[77] From the cytoplasm of enterocytes, glucose is released in the general circulation via, at least, glucose transporter 2 located in the basolateral cytoplasmic membrane of enterocytes. The sodium

gradient necessary for SGLT1 activity is maintained by a basolateral $Na^+/K^+$ ATPase.[78] In spontaneous type 2 diabetic obese KK-Ay mice, the extract given orally at a dose of 500 mg/kg/day decreased nonfasting glycaemia by 28% and triglycerides by 14% ,whereas cholesterolaemia and serum-free fatty acids were not affected.[79] Quercetin inhibited yeast α-glucosidase with $IC_{50}$ value of 58.9 μM (acarbose: 130.7 μM).[80]

## 1.25 *Terminalia bellirica* (Gaertn.) Roxb.

*Synonyms*: *Myrobalanus bellirica* Gaertn.; *Terminalia attenuata* Edgew.; *Terminalia eglandulosa* Roxb. ex C.B. Clarke; *Terminalia gella* Dalzell; *Terminalia laurinoides* Teijsm. & Binn.; *Terminalia punctata* Roth
*Common names*: pi li le (Chinese); vibhitaka (India); belliric myrobalan
Subclass Rosidae, Superorder Myrtanae, Order Myrtales, Family Combretaceae
*Medicinal use*: fever (India)
*History*: The plant was known to Sushruta (circa 600 BC) Ayurvedic physician

Sabu et al. (2009) provided evidence that methanol extract from fruits of *Terminalia bellirica* (Gaertn.) Roxb. (Figure 1.16) given orally to alloxan-induced diabetic Wistar rats at a dose of 100 mg/kg/day for 12 days reduced glycaemia by 37.5%.[81] This regimen brought to normal serum

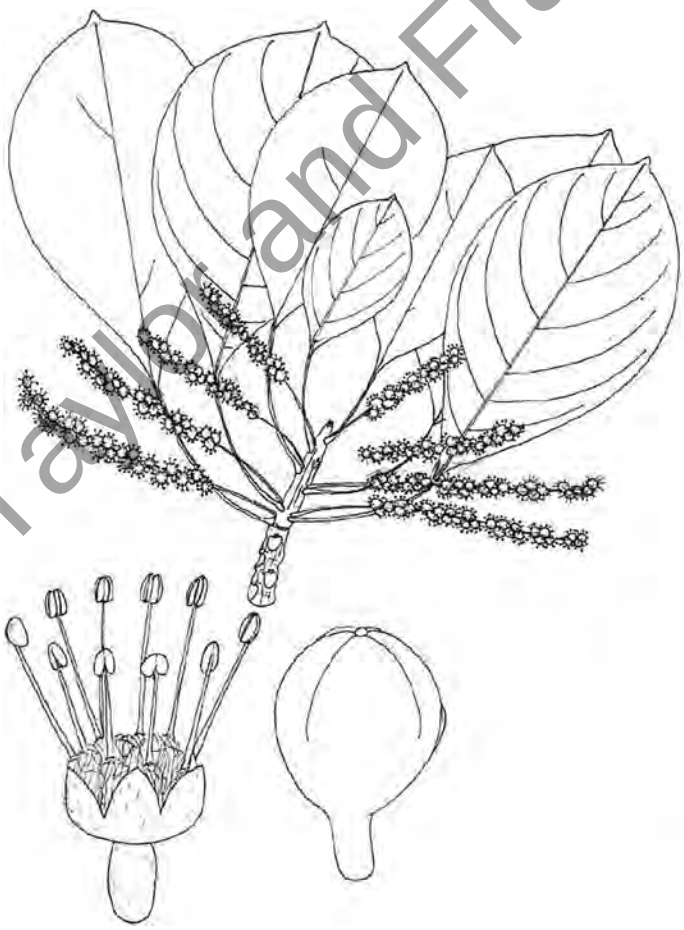


**FIGURE 1.16** *Terminalia bellirica* (Gaertn.) Roxb.

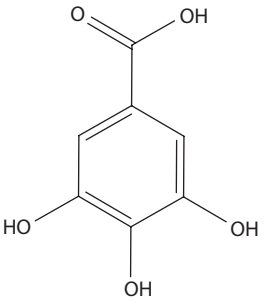



**FIGURE 1.17** Gallic acid.

and hepatic lipid peroxidation and glutathione, whereas catalase, glutathione peroxidase, and superoxide dismutase enzymatic activities were increased.[81] Aqueous extract from fruits of *Terminalia bellirica* (Gaertn.) Roxb. given at 3% of diet to spontaneous type 2 diabetic Tsumura Suzuki Obese Diabetes (TSOD) mice for 8 weeks evoked a mild reduction of body weight and weight of visceral, mesenteric, and subcutaneous fat without reduction of food intake.[82] This supplementation improved glucose tolerance as evidenced by a decrease of peak glycaemia from about 450 to 325 mg/dL after 30 minutes in oral glucose tolerance test.[82] The extract decreased fasting insulinaemia as well as insulin resistance and decreased hepatic triglycerides.[82] In ddY mice, the extract at a dose of 1 g/kg halved peak plasma triglycerides at 4 hours in olive-oil loading test suggesting pancreatic lipase inhibition.[82] The extract inhibited the enzymatic activity pancreatic lipase *in vitro* with an $IC_{50}$ of 65.7 μg/mL and gallic acid (Figure 1.17) isolated from it inhibited the enzymatic activity of pancreatic lipase with an $IC_{50}$ of 3.9 μg/mL.[82] In a subsequent study, gallic acid and methyl gallate, which are produced by members of the genus *Terminalia* L,. inhibited *in vitro* the enzymatic activity of α-glucosidase with $IC_{50}$ values of 5.2 and 11.5 μM, respectively.[83] Gallic acid and methyl gallate are derived from ellagitannins suggesting that α-glucosidase and/or lipase inhibition upon oral loading of ellagitannins can be elicited by gastro-intestinal metabolites.[71] In fact, Espin et al. (2007) fed Iberian pigs with ellagitannins and observed the release of ellagic acid in the jejunum, which was directly absorbed in the first portions of the gastrointestinal tract.[71] The intestinal bacterial commensal flora metabolizes nonabsorbed ellagic acid into benzopyranone derivatives such as urolithin A, which are absorbed.[71]

## 1.26 *Vaccinium myrtillus* L.

*Synonyms*: *Vaccinium oreophilum* Rydb.
*Common names*: hei guo yue ju (Chinese); bilberry
Subclass Dillenidae, Superorder Ericanae, Order Ericales, Family Ericaceae
*Nutritional use*: food (China)

The fruits of *Vaccinium myrtillus* L. accumulate series of anthocyanosides of which delphinidin 3-*O*-β-D-glucopyranoside, cyanidin 3-*O*-β-D-glucopyranoside, peonidin 3-*O*-β-D-glycopyranoside, and malvidin 3-*O*-β-D-glucopyranoside.[84] Methanol extract from fruits of *Vaccinium myrtillus* L. inhibited α-amylase and α-glucosidase with $IC_{50}$ values of 61.3 and 138.4 μg/mL, respectively.[86] Tadeka et al. (2006) provided evidence that cyanidin (Figure 1.18) at a concentration of 500 μM inhibited rat intestinal α-glucosidase and porcine pancreatic α-amylase activity by 6% and 37%, respectively.[86] In this experiment, yeast α-glucosidase was inhibited by 99% at a concentration of 200 μM.[86] In enterocytes, cholesterol is re-esterified in cholesteryl ester by acyl-coenzyme

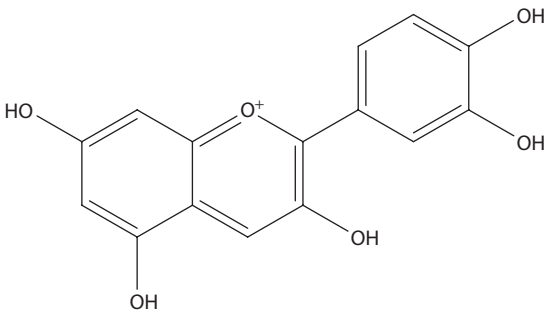



**FIGURE 1.18** Cyanidin-3.

A:cholesterol *O*-acyltransferase-2 (ACAT-2).[87] Anthocyanin fraction of blueberry containing mainly cyanidin-3-*O*-glucoside (Figure 1.18) and petunidin-3-*O*-glucoside added at 1% of diet to Golden Syrian hamsters for 6 weeks decreased plasma cholesterol from 6.6 to 5.8 mmol/L and increased fecal cholesterol implying inhibition of dietary cholesterol absorption as a result of decreased intestinal expression of ACAT-2.[88] In this experiment, plasma triglyceride intestinal absorption was not affected by anthocyanin. Hamsters are good animal models for the study of lipid metabolism because cholesterol metabolism in hamster closely resembles that in human in contrast to rats and mice.[89] The fruits of *Vaccinium myrtillus* L. could be conceptually seen as beneficial ingredient for the diet of subjects with metabolic syndrome.[90,91]

## 1.27 *Lagerstroemia speciosa* (L.) Pers.

*Synonyms*: *Lagerstroemia flos-reginae* Retz.; *Lagerstroemia reginae* Roxb.; *Munchausia speciosa* L.
*Common names*: banaba (Philippines); Queen crape-myrtle
Subclass Rosidae, Superorder Myrtanae, Order Myrtales, Family Lythraceae
*Medicinal use*: diabetes (Philippines)

Faustino Garcia reported in 1941 that dried leaves or ripe fruits of *Lagerstroemia speciosa* (L.) Pers. (Figure 1.19) known in the Philippines as *banaba* at a dose of 20 g in the form decoction had the same activity as 7 units of insulin in decreasing blood glucose. The flowers at the same dose had activity equivalent to 5 units of insulin.[92] Aqueous extract from leaves given orally at a dose of 150 mg/kg/day to streptozotocin-induced diabetic mice for 2 months had no effect up to 10 days treatment but decreased, after 60 days, glycaemia from 119.7 to 63 mg/dL, a value close to 58.1 mg/dL in normoglycaemic rodents.[93] This treatment brought to normal values hepatic lipid peroxidation, glutathione-S-transferase, superoxide dismutase, and glutathione contents.[93] From the leaves of *Lagerstroemia speciosa* (L.) Pers. the triterpenes oleanolic acid, arjunolic acid, asiatic acid, maslinic acid, corosolic acid, and 23-hydroxyursolic acid inhibited α-glucosidase with $IC_{50}$ values below 35 μg/mL.[94,95] Out of these triterpene, corosolic acid inhibited α-amylase with an $IC_{50}$ value of 100 μg/mL.[94,95] Corosolic acid (Figure 1.20) given to spontaneous type 2 diabetic KK-Ay as 0.023% part of a high cholesterol diet for 10 weeks maintained plasma cholesterol to the level of control whereby it had no effect on weight gain.[94] This treatment halved hepatic cholesterol content and decreased cholesterolaemia in oral cholesterol test to about 10% at 4 hours on probable account of ACAT-2 inhibition.[94] Clinical trials are warranted.

**FIGURE 1.19** *Lagerstroemia speciosa* (L.) Pers.

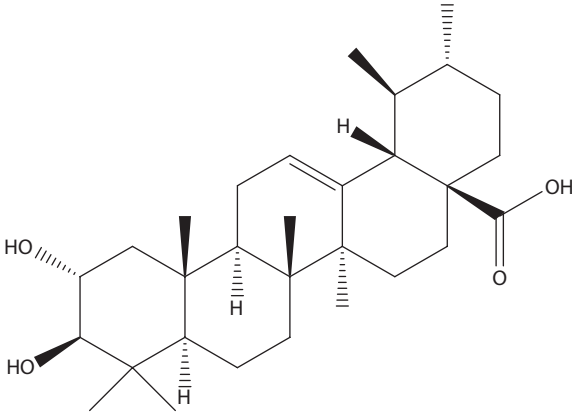



**FIGURE 1.20** Corosolic acid.

## 1.28 *Punica granatum* L.

*Common names*: shi liu (Chinese); dhalim (India); pomegranate
Subclass Rosidae, Superorder Myrtanae, Order Myrtales, Family Lythraceae
*Medicinal use*: diabetes (India)
*History*: The plant was known of twelfth century Arabic physician Serapion as astringent

Ellagitannins in the fruits of *Punica granatum* L. inhibit *in vitro* the intestinal enzymes in charge of carbohydrate and triglyceride absorption. Methanol extract from seeds at a concentration of 2.5 mg/mL inhibited α-amylase activity by 94.5% *in vitro* ($IC_{50}$: 1.1 mg/mL; acarbose: 1.3 μg/mL).[96] Methanol extract from husk of *Punica granatum* L. seeds at a concentration of 2.5 mg/mL inhibited porcine pancreatic lipase by 100% *in vitro* ($IC_{50}$: 0.1 mg/mL; orlistat: 0.1 ng/mL).[96] Punicalagin, punicalin, and ellagic acid isolated from *Punica granatum* L. inhibited *in vitro* rat α-glucosidase with $IC_{50}$ values of 140.2, 191.4, and 380 μmol/L, respectively.[97] Methanol fractions of flowers of *Punica granatum* L. inhibited the enzymatic activity of recombinant human maltase–glucoamylase, rat maltase, and rat sucrase with $IC_{50}$ values equal to 567, 87, and 324 μg/mL.[98] In the same experiment, a methanol fraction of arils inhibited the enzymatic activity of recombinant human maltase–glucoamylase, rat maltase, and rat sucrase with $IC_{50}$ values equal to 393.3, 527, and 486 μg/mL, respectively.[98] From the methanol fraction of aril, oenothein B and punicalagin inhibited human maltase–glucoamylase, rat maltase, and rat sucrase with $IC_{50}$ values equal to 174, 290, 213, 305, 535, and 369 μM, respectively.[98] Consumption fruits' juice of *Punica granatum* L. could be of value for metabolic syndrome.

## 1.29 *Trapa japonica* Flerow

*Synonym*: *Trapa litwinowii* V.N. Vassil.
Subclass Rosidae, Superorder Myrtanae, Order Myrtales, Family Trapaceae
*Medicinal use*: diabetes (India)

A single oral 40 mg/kg administration of a polyphenolic extract isolated from the husk of *Trapa japonica* Flerow to ICR mice receiving a load of starch halved postprandial glycaemia after 30 minutes and reduced plasma insulin.[99] From this extract, eugeniin, 1,2,3,6-tetra-*O*-galloyl-β-D-glucopyranose and (−)-epigallocatechin gallate inhibited the enzymatic activity of human salivary α-amylase with $IC_{50}$ of 42, 58, and 53 μM, respectively.[99] Eugeniin, 1,2,3,6-tetra-*O*-galloyl-β-D-glucopyranose and (−)-epigallocatechin gallate inhibited also maltase with $IC_{50}$ of 69, 83, and 107 μM, respectively, and sucrase with $IC_{50}$ of 333, 260, and 268 μM, respectively.[99]

## 1.30 *Cassia auriculata* L.

*Synonym*: *Senna auriculata* (L.) Roxb.
*Common names*: er ye jue ming (Chinese); avartaki (India); tanner's cassia
Subclass Rosidae, Superorder Fabanae, Subclass Rosiidae, Family Fabaceae
*Medicinal use*: diabetes (India)

Aqueous extract from leaves of *Cassia auriculata* L. given to streptozotocin-induced diabetic Wistar rats at a dose of 400 mg/kg for 21 days reduced fasting glycaemia from 214.2 to 113.8 mg/dL, a value close to a normoglycaemia (82 mg/dL).[100] Further, this treatment normalized serum lipid peroxides, erythrocytes superoxide dismutase, catalase, and glutathion.[100] Ethanol extract of aerial parts *Cassia auriculata* L. inhibited *in vitro* the enzymatic activity of lipase with an $IC_{50}$ value equal to 6 μg/mL.[101] From this plant, kaempferol-3-*O*-rutinoside (Figure 1.21), quercetin, luteolin, and rutin inhibited *in vitro* the enzymatic activity of porcine pancreatic lipase with $IC_{50}$ values equal to 1.7, 49.3, 76.5, and 91 μg/mL, respectively.[101]

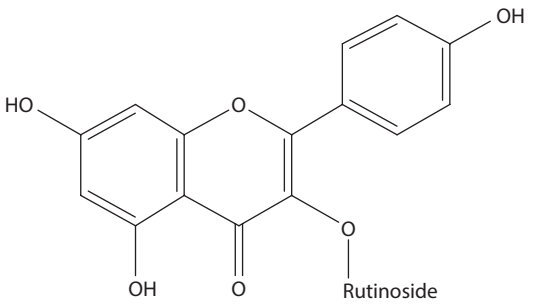



**FIGURE 1.21** Kaempferol-3-*O*-rutinoside.

## 1.31 *Mucuna pruriens* (L.) DC.

*Synonym*: *Dolichos pruriens* L.
*Common names*: atmagupta (India); common cowitch
Subclass Rosidae, Superorder Fabanae, Subclass Rosiidae, Family Fabaceae
*Medicinal use*: tonic (India)

Members of the family Fabaceae synthetize isoflavonoids and pterocarpans that inhibit α-glucosidase *in vitro*. The isoflavanones mucunone A and B, the pterocarpan (6a*R*,11a*R*)-medicarpin, the isoflavanone parvisoflavone B (Figure 1.22), the isoflavans (3R)-vestitol, and 8-methoxyvestitol isolated from the roots of *Mucuna pruriens* (L.) DC. inhibited α-glucosidase with $IC_{50}$ values below 120 μM (acarbose: 7.9 μM).[102]

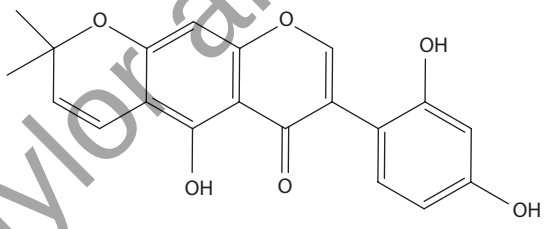



**FIGURE 1.22** Parvisoflavone B.



## 1.32 *Pterocarpus marsupium* Roxb.

*Synonyms*: *Lingoum marsupium* (Roxb.) Kuntze; *Pterocarpus bilobus* Roxb. ex G. Don
*Common names*: ma la ba zi tan (Chinese); kum kusrala (India); kino
Subclass Rosidae, Superorder Fabanae, Subclass Rosiidae, Fabaceae
*Medicinal use*: diabetes (India)
*History*: The plant was known to Sushruta

The plant yields an exudate called East Indian kino that has been used for the treatment of diarrhea. Abesunadara et al. (2004) made the demonstration that the exudate of *Pterocarpus marsupium*

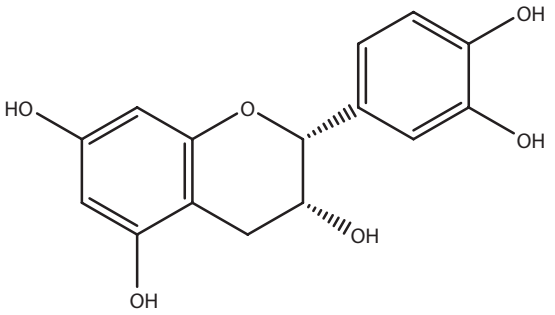



**FIGURE 1.23** (–)-Epicatechin.

Roxb. was able to inhibit α-glucosidase *in vitro* on probable account of (–)-epicatechin (Figure 1.23) and catechin[104]. (–)-Epicatechin inhibited *in vitro* the enzymatic activity of α-glucosidase with an $IC_{50}$ of 5.8 μg/mLs.[103,104]

## 1.33 *Polygala aureocauda* Dunn

*Synonym*: *Polygala fallax* Hemsl.
*Common name*: huang hua dao shui lian (Chinese)
Subclass Rosidae, Superorder Fabanae, Order Polygalales, Family Polygalaceae
*Nutritional use*: food (China)

Reinioside C from the roots of *Polygala aureocauda* Dunn given at a dose of 16 mg/kg/day for 30 days orally to Kunming mice on hyperlipidemic diet attenuated plasma cholesterol from 5.6 to 4 mmol/L, normalized plasma triglycerides from 1.1 to 0.8 mmol/L.[105,107] Besides, this pentacyclic triterpene saponins lowered hepatic cholesterol and brought hepatic triglycerides to normal values and these effects were comparable to simvastatin (4 mg/kg/days).[105] Decrease in serum and hepatic cholesterol is, at least, an indication of decreased absorption of cholesterol in small intestine or increased fecal excression of bile acids in the feces. Triterpene saponins and steroidal glycosides found in medicinal plants in Asia have the tendency to form insoluble stoichiometric complexes with cholesterol *in vitro* and interact with bile acid micelles expelling cholesterol from them, thereby inhibiting cholesterol absorption and decreasing serum cholesterol.[106]

## 1.34 *Citrus limon* (L.) Osbeck

*Synonym*: *Citrus limonum* Risso
*Common names*: limau (Malay); lemon
Subclass Rosidae, Superorder Rutanae, Order Rutales, Family Rutaceae
*Medicinal use*: high cholesterol (Malaysia)

Kawaguchi et al. (1997) provided evidence that hesperidin and neohesperidine that occur in the peels of fruits of *Citrus limon* (L.) Osbeck (Figure 1.24) inhibited porcine pancreatic lipase with $IC_{50}$ values of 32 and 46 μM, respectively, whereas narirutin and narigin were inactive.[108] Hesperidin given as part of 10% diet to rats had no effect on body weight, increased fecal lipids from 0.09 to 1 g/3days and decreased plasma triglycerides from 89.5 to 64.1 mg/dL.[108]

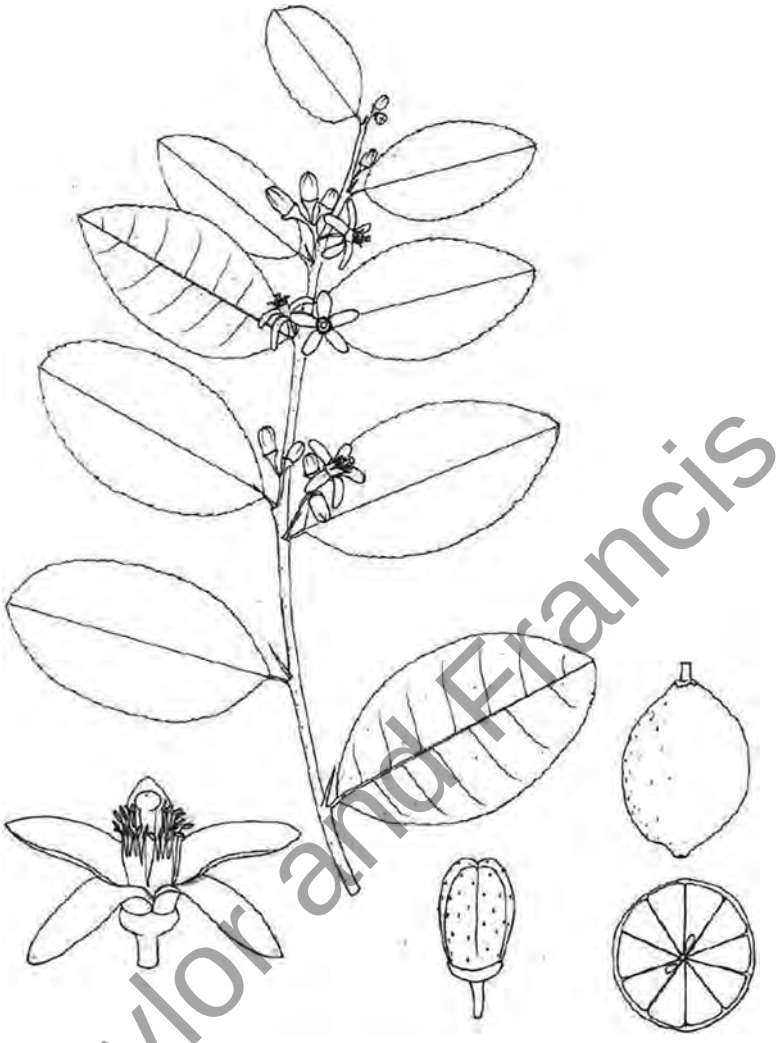


**FIGURE 1.24** *Citrus limon* (L.) Osbeck.



## 1.35 *Murraya koenigii* (L.) Spreng.

*Synonyms*: *Bergera koenigii* L.; *Chalcas koenigii* (L.) Kurz
*Common names*: tiao liao jiu li xiang (Chinese); karivepu (India); daun kari (Malay); curry leaf tree
Subclass Rosidae, Superorder Rutanae, Order Rutales, Family Rutaceae
*Medicinal use*: indigestion (India)

Carbazole alkaloids elaborated by members of the family Rutaceae have the ability to inhibit α-glucosidase and/or intestinal lipase. The dimeric carbazole alkaloids bisgerayafolines A, B, and C isolated from the fruits of *Murraya koenigii* (L.) Spreng. inhibited the enzymatic activity of α-glucosidase with $IC_{50}$ values equal to 45.4, 41.2, and 69 μM, respectively.[109] Dichloromethane

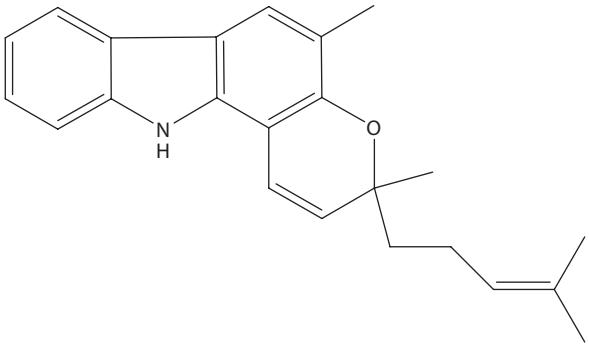



**FIGURE 1.25** Mahanimbine.

extract from leaves of *Murraya koenigii* (L.) Spreng. given orally at a dose of 300 mg/kg for 2 weeks to rodents fed with high-fat diet reduced weight gain from 64.2 to 14.6 g compared to control.[110] In the same experiment serum total cholesterol and triglycerides from 117.8 and 178.3 mg/dL to 79.7 mg/dL and 121.9 mg/dL, respectively, whereby glycaemia was unchanged.[110] Mahanimbine from this extract at a dose of 30 mg/kg/day inhibited weight gain in high-fat fed rodents and reduced plasma cholesterol and triglycerides to 98.2 and 130.2 mg/dL.[110] Mahanimbine (Figure 1.25) and koenimbin from *Murraya koenigii* (L.) Spreng. inhibited the enzymatic activity of lipase with $IC_{50}$ values equal to 17.9 and 168.6 μM, respectively.[111]

## 1.36 *Zanthoxylum piperitum* DC.

Subclass Rosidae, Superorder Rutanae, Order Rutales, Family Rutaceae
*Common name*: Japanese pepper
*Medicinal use*: indigestion (China)

In enterocytes, dietary cholesterol is re-esterified into cholesteryl ester by acyl-CoA:cholesterol *O*-acyltransferase-2.[87] The aliphatic amides β-Sanshool and γ-sanshool isolated from the stems of *Zanthoxylum piperitum* DC. (Figure 1.26) inhibited the enzymatic activity of human acyl-CoA:cholesterol *O*-acyltransferase-2 with $IC_{50}$ values of 79.7 and 82.6 μM, respectively.[112]

**FIGURE 1.26** *Zanthoxylum piperitum* DC.



## 1.37 *Cedrela odorata* L.

Subclass Rosidae, Superorder Rutanae, Order Rutales, Family Meliaceae

Ethanolic extract of inner stembark of *Cedrela odorata* L. (containing gallic acid, (−)-gallocatechin and (+)-catechin) inhibited α-glucosidase with an $IC_{50}$ of 84.7 μg/mL (acarbose 5.1 μg/mL).[113] Given to streptozotocin-induced diabetic Wistar rats at a single oral dose of 500 mg/kg, 30 minutes prior to oral lead of glucose decreased postprandial glycemia from about 500 to 255 mg/dL and delayed peak glycaemia from 45 to 90 minutes.[113] Given to streptozotocin-induced diabetic Wistar rats at a single oral dose of 500 mg/kg 30 minutes prior to oral lead of sucrose or starch decreased postprandial glycemia at 30 minutes to a lesser extent, suggesting that the extract may also be inhibiting glucose transporters in the intestine by blocking inhibited $Na^+$-glucose cotransporter-1 (SGLT1).[113] However, 500 mg/kg given daily for 30 days had no beneficial effects on glycaemia.[113]

## 1.38 *Mangifera indica* L.

*Common names*: am (India); mango
Subclass Rosidae, Superoder Rutanae, Order Rutales, Family Anacardiaceae
*Medicinal use*: diabetes (India)

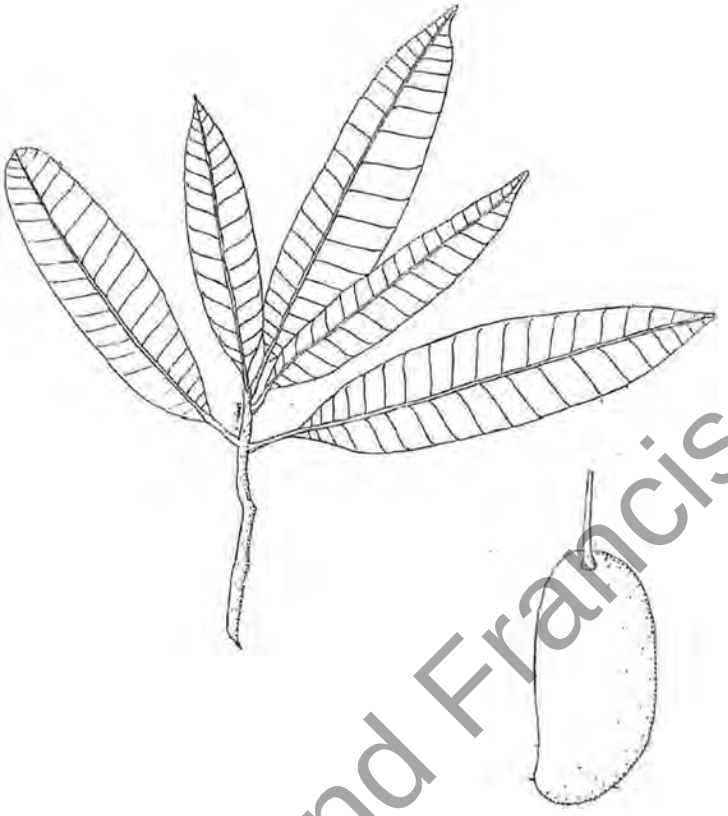


**FIGURE 1.27** *Mangifera indica* L.



Ethanol extract from bark of *Mangifera indica* L. (Figure 1.27) at a concentration of 500 µg/mL inhibited α-glucosidase activity by 64.9% ($IC_{50}$: 314 µg/mL), whereby acarbose at 0.8 µg/mL evoked a 62.4% inhibition.[114] The natural product involved here is to date apparently unknown but one could suggest the involvement of phenolics of which possibly the xanthone glycoside mangiferin or gallotannin, which abounds in the plant.[114]

## 1.39 *Pistacia chinensis* Bunge

*Synonyms*: *Pistacia formosana* Matsumura; *Pistacia. Philippinensis* Merrill & Rolfe; *Rhus argyi* H. Léveillé; *Rhus. Gummifera* H. Léveillé.
*Common names*: huang lian mu (Chinese); karkata (India)
Subclass Rosidae, Superoder Rutanae, Order Rutales, Family Anacardiaceae
*Medicinal use*: dysentery (India)

Galls of *Pistacia chinensis* Bunge contains the triterpene pistagremic acid (Figure 1.28) that inhibited yeast α-glucosidase and rat intestinal α-glucosidase activities with $IC_{50}$ values equal to 89.1 and 62.4 µM, respectively. This triterpene was more potent than acarbose ($IC_{50}$: 780.2 and 38.9 µM) against yeast α-glucosidase and rat-intestinal α-glucosidase.[115] Aqueous extract from aerial parts of a member of the genus *Pistacia* at 50 mg/mL inhibited glucose liberation from starch by α-amylase and α-amyloglucosidase by 60%.[116] This extract intragastrically given to Sprague–Dawley rats at a dose of 500 mg/kg decreased peak glycaemia at 45 minutes in oral

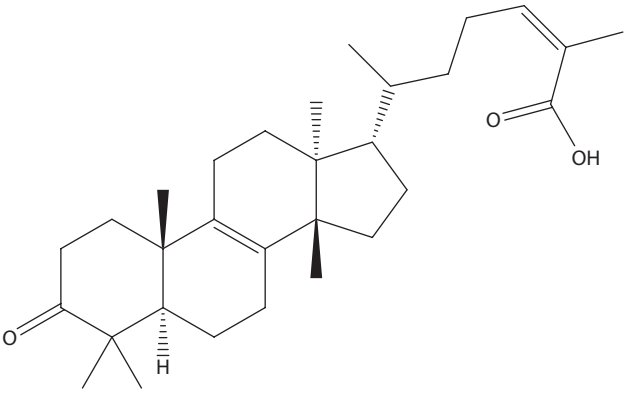



**FIGURE 1.28** Pistagremic acid.

starch tolerance test from about 6.5 to 5.5 mM, and this effect was close to 3 mg/kg of acarbose (5 mM).[116] At the same dosage, this extract decreased 90 minutes glycaemia peak from about 6.3 to 5.5 mmol/L.[116]

## 1.40 *Salacia oblonga* Wall.

Subclass Rosiidae, Superorder Celastranae, Order Celastrales, Family Celastraceae
*Medicinal use*: diabetes (India)

William et al. (2007) observed that extract of *Salacia oblonga* Wall. given at a dose of 480 mg/kg during meal tolerance test decreased postprandial glycaemia peak at 120 minutes by 27% in patients with type 2 diabetes and decreased peak serum insulin by 12%.[117] In a subsequent study, aqueous extract of roots of *Salacia oblonga* Wall. (containing mangiferin) given orally to mice at a single dose of 100 mg/kg 1 hour before sucrose loading decreased postprandial plasma glucose at 30 minutes more efficiently than acarbose at 200 mg/kg and had no effect of postprandial glycemia following glucose loading.[118] The extract inhibited α-glucosidase activity *in vitro* with an $IC_{50}$ of 5.2 μg/mL, whereas mangiferin and acarbose show much weaker effects with $IC_{50}$ of 22.7 and 53.9 μg/mL, respectively.[118] From this extract kotalagenin 16 acetate, maytenfolic acid, 3β, 22α-dihydroxyoleanane-12-en-29-oic acid, 19-hydroxyferruginol, and lambertic acid inhibited α-glucosidase.[119]

## 1.41 *Salacia reticulata* Wight

Subclass Rosiidae, Superorder Celastranae, Order Celastrales, Family Celastraceae
*Medicinal use*: diabetes (Sri Lanka)

Karunanayake et al. (1984) administered aqueous extract from root bark of *Salacia reticulata* Wight at a single dose of 1 mL/100 g to Sprague–Dawley rats and observed a fasting blood glucose decrease by 30%, 1 hour after administration implying at least, an increase of insulin secretion, inhibition of liver secretion of glucose, or increase uptake of glucose by peripheral tissues.[120]

Aqueous extract from roots of *Salacia reticulata* Wight. given orally to Zucker fatty rats at a dose of 125 mg/kg/day for 27 days evoked a decrease in body weight of 14%.[121] From this extract, (−)-epigallocatechin, (−)-epicatechin-(4β→8)-(−)-4-*O*-methylepigallocatechin, and lambertic acid inhibited porcine pancreatic lipase with $IC_{50}$ values of 88, 68, and 225 mg/mL, respectively, *in vitro*.[121] Aqueous extract from leaves of *Salacia reticulata* Wight. at a concentration of 400 µg/m inhibited *in vitro* intestinal rat α-glucosidase by 78.5%.[122] In ddY mice, the extract given orally at a single dose of 1 mg with 160 mg of maltose or sucrose decreased postprandial glycaemia.[122] In the same experiment performed with 160 mg of glucose, the extract had no effect on postprandial glycaemia.[122] In streptozotocin-induced diabetic mice, the extract mixed with drinking water to 0.01% for 4 days lowered glycaemia and the enzymatic activity of intestinal maltase and sucrase.[122] *Salacia reticulata* Wight. proven nontoxic could be of value for the treatment of metabolic syndrome.

## 1.42 *Viscum album* L.

Subclass Rosiidae, Superorder Santalanae, Order Santalales, Family Viscaceae
*Medicinal use*: atherosclerosis (Turkey)

Ethanol extract from *Viscum album* L. inhibited *in vitro* the enzymatic activity of pancreatic lipase with an $IC_{50}$ value equal to 33.3 µg/mL.[8] Aqueous extract from the plant given orally at a dose of 100 mg/kg to Swiss albino mice on high-cholesterol diet decreased plasma cholesterol from 218.4 to 139.4 mg/dL and decreased plasma triglycerides from 194.2 to 63.6 mg/dL.[124] This extract also decreased glycemia from 79.8 to 54.6 mg/dL.[123] This parasitic plant well-known of Celts elaborates β-Amyrin acetate, oleanolic acid, betulinic acid, phytosterol, as well as quercetin methyl ethers.[124,125]

## 1.43 *Viburnum dilatatum* Thunb.

*Synonyms*: *Viburnum brevipes* Rehder; *Viburnum fulvotomentosum* P.S. Hsu
*Common name*: jia mi (Chinese)
Subclass Asteridae, Superorder Cornanae, Order Dipsacales, Family Viburnaceae
*Medicinal use*: sores (China)

Lyophilized fruits' juice of *Viburnum dilatatum* Thunb. (Figure 1.29) given to streptozotocin-induced diabetic Sprague–Dawley rats in drinking water at a concentration of 16.8 mg/mL for 10 weeks had no effects on food consumption but attenuated body weight loss.[126] This supplementation decreased plasma glucose from 2 to 1.5 mmol/L (normal: 1.3 mmol/L), normalized plasma cholesterol from 1.1 to 0.5 mg/mL (normal: 0.6 mg/mL), and triglycerides from 1.6 to 1.2 mg/mL (normal: 1.3 mg/mL).[126] The regimen had no effect on insulin.[126] Lyophilized fruits' juice of *Viburnum dilatatum* Thunb. given to streptozotocin-induced diabetic Sprague–Dawley rats orally at a dose of 500 mg/kg/day for 4 weeks had no effect on body weight loss, decreased postprandial glycemia in oral glucose tolerance test, and had no effect on plasma insulin.[127] From this juice, cyanidin 3-sambubioside inhibited rat sucrase, maltase, isomaltase, glucoamylase, and porcine pancreatic a-amylase with $IC_{50}$ values below 15 mM.[127] Also from this juice, cyanidin 3-*O*-glucoside inhibited rat sucrase, maltase, isomaltase, glucoamylase, and porcine pancreatic α-amylase with $IC_{50}$ values below 110 mM.[127] 5-Caffeoyl quinic acid from the juice inhibited rat sucrase, maltase, isomaltase, glucoamylase, and porcine pancreatic a-amylase with $IC_{50}$ values of 1.4, 24.8, 23.4, 5, and 37.1 mM, respectively.[127]

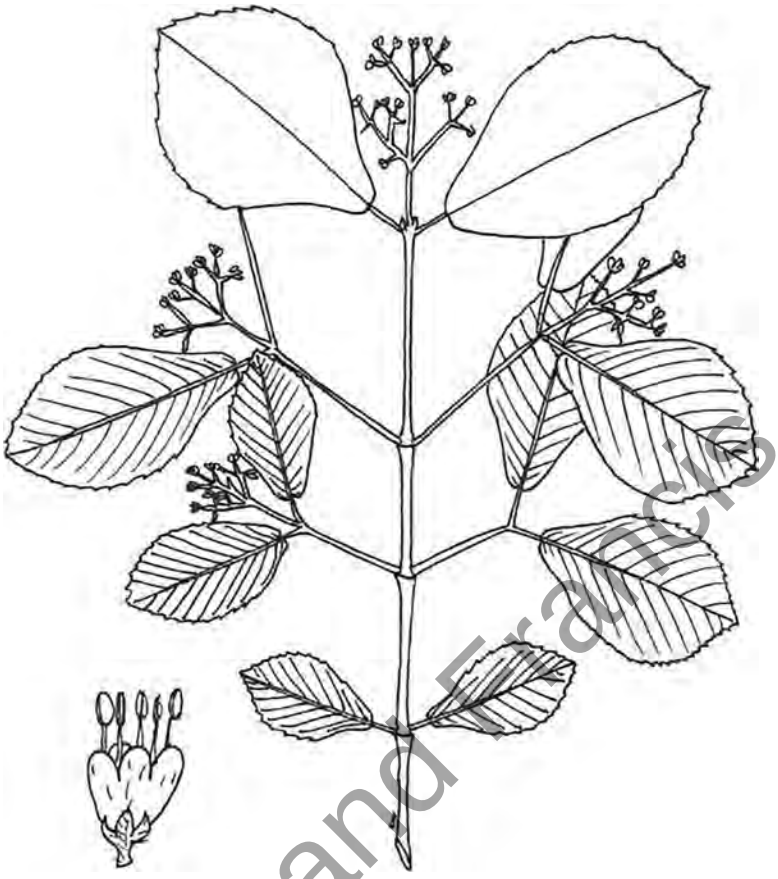


**FIGURE 1.29** *Viburnum dilatatum* Thunb.



## 1.44 *Lonicera coerulea* L.

Subclass Asteridae, Superorder Cornanae, Order Dipsacales, Family Caprifoliaceae
*Medicinal use*: inflammation (China)

Anthocyanin fraction of fruits of *Lonicera coerulea* L. (containing 87.5 mg/100 mg of cyanidin 3-glucoside) given to C57BL/6 mice at a dose of 200 mg/kg of high-fat diet for 16 weeks had no effect on food intake, evoked a reduction of body weight gain by 24.1% compared to untreated animals (orlistat 100 mg/kg: 16.9%), and evoked a mild reduction of epididymal fat mass.[128] This regimen decreased plasma glucose and triglycerides, had no effect of total plasma cholesterol and decreased parameter of liver injury.[128] This fraction decreased hepatic triglycerides.[128] The supplementation decreased plasma insulin as efficiently as orlistat, halved plasma leptin and decreased insulin resistance to normal levels.[128] In general, a decrease in plasma insulin implies an increase in insulin sensitivity. This set of data suggests that the consumption of fruits of *Lonicera coerulea* L. could assist in treating metabolic syndrome. Clinical studies are needed.

## 1.45 *Ilex cornuta* Lindl. & Paxton

Subclass Asteridae, Superorder Cornananae, Order Aquifoliales, Family Aquifoliaceae
*Medicinal use*: fatigue (China)

Triterpenes have the tendency to inhibit acyl-CoA:cholesterol transferase-2 which regulates cholesterol absorption in enterocytes.[87] In fact triterpenes are structurally close to cholesterol. For instance, *Ilex cornuta* Lindl. & Paxton contains the lupane triterpene lupeol (Figure 1.30), which at a concentration of 100 μM inhibited the enzymatic activity of acyl-CoA:cholesterol transferase-2 (hACAT-2) by 48.2%.[129,130] In a subsequent study, Baek et al. (2010) tested lupeol against acyl-CoA:cholesterol transferase-2 and found an $IC_{50}$ of $13.8 \times 10^{-2}$ mM, whereas lupan-type triterpene betulinic acid had $IC_{50}$ of $13.8 \times 10^{-2}$ mM. In this experiment, the oleanane-type triterpene oleanolic acid was mildly active with 22% inhibition at a concentration of 50 μg/mL compared to untreated group.[131] Lupeol inhibited α-glucosidase with an $IC_{50}$ value equal to 6.2 μg/mL.[131]

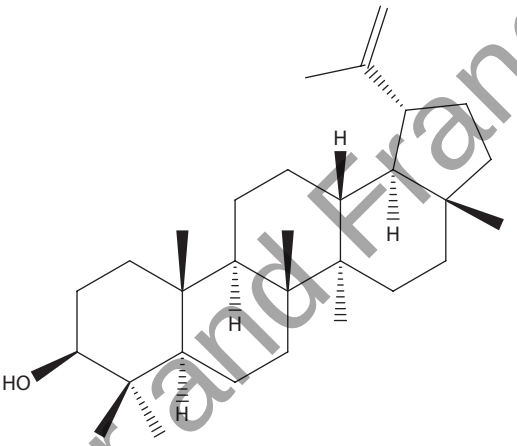



**FIGURE 1.30** Lupeol.

## 1.46 *Acanthopanax senticosus* (Rupr. ex Maxim.) Harms

*Synonyms*: *Eleutherococcus senticosus* (Rupr. ex Maxim.) Maxim.; *Hedera senticosa* Rupr. ex Maxim.
*Common names*: ci wu jia (Chinese); Siberian ginseng
Subclass Asteridae, Superorder Cornanae, Order Apiales, Family Araliaceae
*Medicinal use*: fatigue (China)

*Acanthopanax senticosus* (Rupr. ex Maxim.) Harms is an example of medicinal plant producing a broad array of natural products with inhibitory activity on intestinal enzymes of carbohydrate and triglycerides absorption. The lupane-type saponin 22α-hydroxychiisanoside and the flavanol (+)-afzelechin (Figure 1.31) isolated from the leaves of *Acanthopanax senticosus* (Rupr. ex Maxim.) Harms inhibited α-glucosidase *in vitro* with $IC_{50}$ values equal to 819, and 186 μM, respectively (acarbose $IC_{50}$ 788.6 μM).[132] Silphioside F, copteroside B, hederagenin

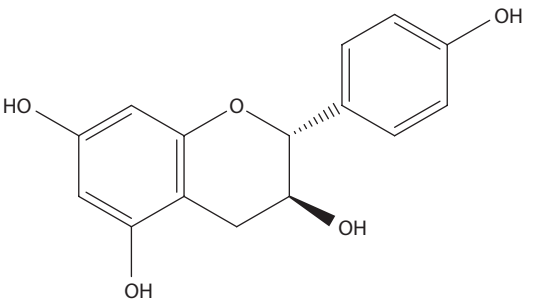



**FIGURE 1.31** (+)-Afzelechin.

3-*O*-β-D-glucuronopyranoside 6′-*O*-methyl ester, and gypsogenin 3-*O*-β-D-glucuronide isolated from the fruits of this plant inhibited *in vitro* porcine pancreatic lipase more efficiently than orlistat.[133] From the same plant, erythro-7 *E*-4',9'-dihydroxy-4,5'-dimethoxy-5,8'-oxyneolign-7-en-9-al isolated inhibited the enzymatic activity of diacylglycerol acyltransferase-1 with an $IC_{50}$ value of 66.5 mM and was inactive against diacylglycerol acyltransferase-2.[134] In brush border enterocytes, short-chain fatty acids penetrate freely, whereby long-chain fatty acids are transported via fatty-acid translocase and fatty-acid transporter protein.[135] In enterocytes, monoacylglycerol transferase catalyzes the formation of diacylglycerol from monoacylglycerol and fatty acids and diacylglycerol acyltransferase-1 catalyze the formation of triglycerides from diacylglycerol. Triglycerides, cholesteryl ester, and apolipoprotein B48 are then packed into chylomicrons via the microsomal transfer protein, which are secreted into the lymphatic system.[135]

## 1.47 *Panax japonicus* (Nees) C.A Meyer

*Synonym*: *Aralia japonica* (Nees) Makino
*Common name*: zhu jie shen (Chinese)
Subclass Asteridae, Superorder Cornanae, Order Apiales, Family Araliaceae
*Medicinal use*: cough (Japan)

The polyacetylene (3S,10S)-panaxydiol (Figure 1.32) isolated from the roots of *Panax japonicas* (Nees) C.A Meyer inhibited yeast α-glucosidase with an $IC_{50}$ of 22.2 μM (acarbose: $IC_{50}$: 677.9 μM).[136] Such compounds are common in members of the Family Apiaceae, Araliaceae and Asteraceae.

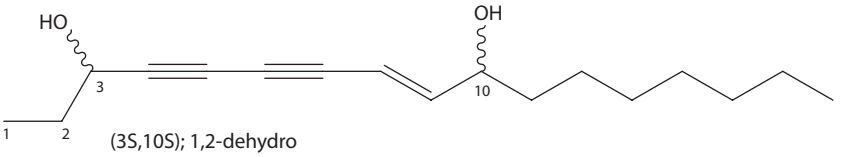



**FIGURE 1.32** (3S,10S)-Panaxydiol.

## 1.48 *Centella asiatica* (L.) Urb.

*Synonyms*: *Centella biflora* (P. Vell.) Nannf.; *Hydrocotyle asiatica* L.; *Hydrocotyle biflora* P. Vell.
*Common names*: pegaga (Malay/Indonesian); Asiatic pennywort
Subclass Cornanae, Superoder Cornanae, Order Apiales, Family Apiaceae
*Nutritional use*: Vegetable (Malaysia)

Ethanol extract of *Centella asiatica* (L.) Urb. inhibited *in vitro* porcine pancreatic lipase, porcine pancreatic α-amylase and yeast α-glucosidase with $IC_{50}$ of 759.1 μg/mL (orlistat: 0.6 μg/mL) 536.5 μg/mL (acarbose: 113.2 μg/mL) and 42.2 μg/mL (acarbose: 34 μg/mL), respectively.[137] Rutin isolated from this extract inhibited *in vitro* porcine pancreatic lipase, porcine pancreatic α-amylase, and yeast α-glucosidase with $IC_{50}$ value of 1412.2 μg/mL (orlistat: 0.6 μg/mL), 513 μg/mL (acarbose: 113.2 μg/mL), and 47 μg/mL (acarbose: 34 μg/mL), respectivey.[137] Following oral load of a lipid emulsion to Wistar rats, the extract at a single oral dose of 1000 mg/kg or rutin (Figure 1.33) lowered postprandial increase in serum triglycerides and total cholesterol.[137]

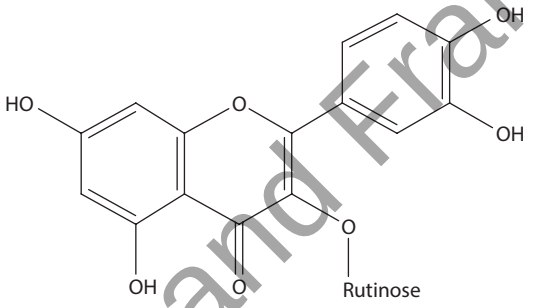



**FIGURE 1.33** Rutin.

## 1.49 *Cnidium officinale* Makino

Subclass Asteranae, Superorder Cornanae, Order Apiales, Family Apiaceae
*Medicinal use*: blood stasis (Korea)

The phthalide derivative senkyunolide B from the rhizome of *Cnidium officinale* Makino inhibited the enzymatic activity of porcine pancreatic lipase with $IC_{50}$ value equal to 86.4 μM.[138] Another example of phtalide derivative of Apiaceae acting on carbohydrate absorption is 3-(Z)-butylidenephthalide that given to rodent orally at a dose of 56 mg/kg inhibited sucrose absorption by about 55% at 30 minutes peak.[139] 3-(Z)-butylidene phthalide inhibited the enzymatic activity of yeast α-glucosidase with a Ki of 4.8 mM (acarbose 0.4 mM).[139]

## 1.50 *Ducrosia anethifolia* DC.

Subclass Asteridae, Superorder Cornanae, Order Apiales, Family Apiaceae
*Medicinal use*: fatigue (Pakistan)

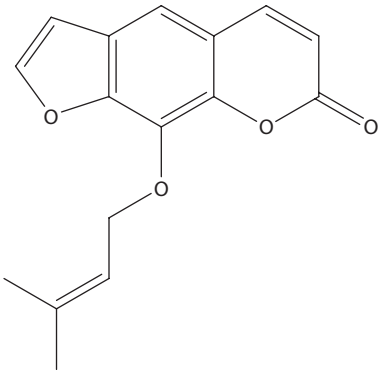


**FIGURE 1.34** Imperatonin.

Defatted ethanol extract of aerial parts of *Ducrosia anethifolia* DC. at a concentration of 10 µg/mL inhibited *in vitro* α-amylase and α-glucosidase by 31.2% and 28.8%, respectively (acarbose 10 µg/mL: 32.2% and 29.9%, respectively).[140] From this extract, imperatorin (Figure 1.34) at a concentration of 10 µg/mL inhibited *in vitro* α-amylase and α-glucosidase by 28.2% and 28.8%, respectively.[140] The extract given orally to streptozotocin-induced diabetic rats (fasting blood glucose >300 mg/dL) at a daily dose of 500 mg/kg for 45 days decreased glycaemia from 365 to 165.6 mg/dL (normal: 111.5 mg/dL) and ameliorated serum cholesterol and triglycerides.[140] Rats with fasting blood glucose between 120 and 250 mg/dL are considered as mildly diabetic, whereas rats with a fasting blood glucose value of 300 mg/dL or more are severely diabetic.[141] Severe diabetes in rats suggests massive pancreatic insults by alloxan and streptozotocin.

## 1.51 *Peucedanum japonicum* Thunb.

*Synonym*: *Anethum japonicum* (Thunb.) Koso-Pol.
*Common name*: bin hai qian hu (Chinese)
Subclass Asteridae, Superorder Cornanae, Order Apiales, Family Apiaceae
*Medicinal use*: cough (Japan)

Ethanol extract of leaves and stems of *Peucedanum japonicum* given to C57BL/6 mice as part of 0.8% of diet for 4 weeks had no effect on food intake, decreased white adipose tissue from 8.3 to 5 g and plasma triglyceride from 60.2 to 39.3 g.[142] Liver triglycerides were reduced from 34.9 to 21.4 mg/dL and fecal triglycerides were increased from 0.3 to 0.5 mg/day.[142] This extract inhibited the activity of pancreatic lipase by 70% at a concentration of 3 mg/mL.[142]

## 1.52 *Platycodon grandiflorus* (Jacq.) A. DC.

*Synonyms*: *Platycodon glaucum* (Thunb.) Nak.
*Common name*: jie geng (Chinese)
*Medicinal use*: cough (Korea)

Saponin fraction of roots of *Platycodon grandiflorus* (Jacq.) A. DC. (containing Platycodin D 25.1 mg/g) given as part of diet (0.5 g/100 g diet) for 6 weeks reduced food intake, prevented weight loss, decreased fasting plasma glucose by 37%, and improved glucose tolerance in diabetic rodents (db/db mice).[143] This regimen reduced the activity of maltase and sucrase by 41%.[143] *In vitro*, the fraction inhibited yeast α-glucosidase activity by 79% at concentrations of 10 mg/mL. In addition, the fraction was a more effective α-glucosidase inhibitor than acarbose at the same concentration

and this effect was superior to acarbose at 5 mg/mL.[143] Db/db mice have a mutated leptin-receptor gene resulting in the increase of food intake and used as a model of obesity and diabetes. These mice are obese, hyperglycemic, hyperlipidemic, have increased plasma insulin and insulin resisitance.[144] *Platycodon grandiflorus* (Jacq.) A. DC. could be of value in the treatment of metabolic syndrome and clinical trials are warranted.

## 1.53 *Artemisia herba-alba* Asso

*Common names*: sheeh (Pakistan); worm wood
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: fatigue (Pakistan)

Extract of *Artemisia herba-alba* Asso given orally to C57BL/6J on high-fat diet mice for 18 weeks at a dose of 2 g/kg decreased glycaemia from about 230 to 139.5 mg/mL (normal: 120 mg/mL), reduced weight gain, reduced plasma insulin from 3.3 to 1.7 ng/mL, and reduced plasma triglycerides and cholesterol to normal values.[145] The plant shelters chlorogenic acid, 4,5-di-caffeoylquinic acid, 3,5-di-caffeoylquinic acid, 4-caffeoylquinic acid, as well as vicenin-2 and isovitexin.[146]

## 1.54 *Carthamus tinctorius* L.

*Common names*: hong hua (Chinese); kusum (India); safflower
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: blood stasis (China).

The seeds of *Carthamus tinctorius* L. contains *N*-p-coumaroyl serotonin and *N*-feruloyl serotonin that inhibited yeast α-glucosidase with $IC_{50}$ values equal to 47.2 and 100 μM, respectively.[147] In the same experiment, serotonin inhibited the enzymatic activity of α-glucosidase by 25.6% at 300 mM suggesting that the aforementioned property is owed to the phenolic moiety.[147]

## 1.55 *Chromolaena odorata* (L.) R.M. King & H. Rob.

*Synonym*: *Eupatorium odoratum* L.
*Common names*: fei ji cao (Chinese); Siam weed
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: diabetes (India)

16-Kauren-19-oic acid (Figure 1.35) isolated from the roots of *Chromolaena odorata* (L.) R.M. King & H. Rob. inhibited yeast α-glucosidase with an $IC_{50}$ value of 23.7 μM (In fact most inhibitors of α-glucosidase isolated so far from medicinal plants are phenolics and triterpenes acarbose $IC_{50}$: 780 μM).[148]

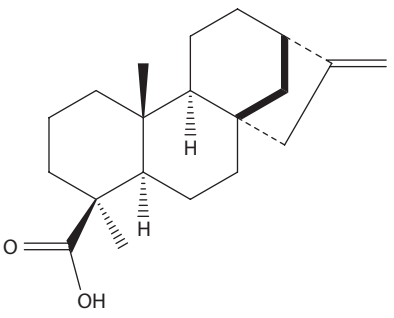



**FIGURE 1.35** 16-Kauren-19-oic acid.

## 1.56 *Cichorium intybus* L.

*Common names*: ju ju (Chinese); kaasani (India); chicory
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: jaundice (India)

18α,19β-20(30taraxasten-)-3β,21α-diol and vanillic acid (Figure 1.36) isolated from the seeds of *Cichorium intybus* L. inhibited yeast α-glucosidase with $IC_{50}$ values of 51.9 and 69 μM, respectively.[149] Roots of *Cichorium intybus* L. contain inulin-type fructans, and in rats, a decrease in plasma triglycerides and cholesterol have been reported after oral administration of fructans.[150,151]

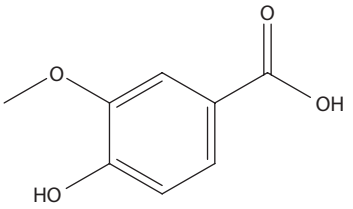



**FIGURE 1.36** Vanillic acid.



## 1.57 *Chrysanthemum morifolium* Ramat

*Synonyms*: *Dendranthema grandiflorum* (Ramat.) Kitam.; *Tanacetum morifolium* Kitam.
*Common names*: ju hua (Chinese); chrysanthemum
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: fever (China)

10α-Hydroxy-1α,4α-peroxide-2-guaien-12,6α-olide, acacetin-7-*O*-β-D-glucopyranoside, acacetin-7-*O*-α-L-rhamnopyranoside flowers of *Chrysanthemum morifolium* inhibited a-glucosidase with $IC_{50}$ values of 229.3, 451.8, and 362.5 μM (acarbose: $IC_{50}$ value of 1907 μM).[152] Eriodictyol, acacetin-7-*O*-β-D-glucopyranoside, acacetin-7-*O*-α-L-rhamnopyranoside inhibited α-amylase with $IC_{50}$ values of 318.2, 337.1, and 112.5 μM (acarbose: $IC_{50}$ value 732.4 μM).[152] 10α-Hydroxy-1α,4α-peroxide-2-guaien-12,6α-olide inhibited porcine pancreatic lipase with an $IC_{50}$ value of 161 μM (orlistat: 108.3 μM).[152]

## 1.58 *Cynara scolymus* L.

*Synonym*: *Cynara cardunculus* L.
*Common name*: artichoke
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Nutritional use*: Vegetable (Turkey)
*History*: The plant was known Dioscorides

Methanol extract of leaves of *Cynara scolymus* L. given orally to mice at a single dose of 500 mg/kg 30 minutes before olive oil loading reduced plasma triglycerides after 2 hours from about 300 to 100 mg/dL (normal: about 110 mg/dL; orlistat 250 mg/kg: 100 mg/dL).[153] From this extract, the sesquiterpenes aguerine B, grosheimin, cynaropicrin, and the flavone glycoside luteolin

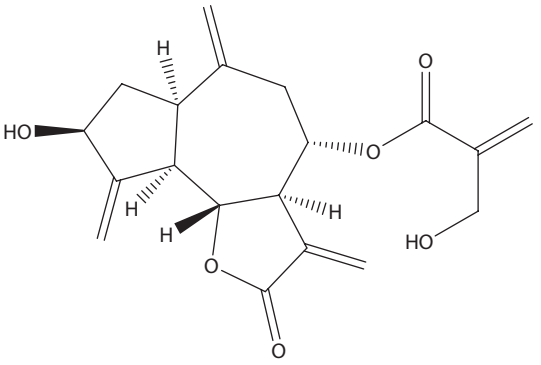



**FIGURE 1.37** Cynaropicrin.

7-*O*-β-D-glucopyranoside given orally to mice at a single dose of 100 mg/kg 30 minutes before olive-oil loading reduced plasma triglycerides after 2 hours from about 450 to 150 mg/dL, 500 to 200 mg/dL, 500 to 150 mg/dL, and 500 to 300 mg/dL.[153] Aguerine B, grosheimin, cynaropicrin (Figure 1.37) and luteolin 7-*O*-β-D-glucopyranoside were, in this study, not active against pancreatic lipase but delayed gastric emptying in oral olive-oil load.[153] In contradiction to this, a subsequent study reported that ethanol extract from leaves of *Cynara scolymus* L. at a concentration of 100 µg/mL inhibited porcine pancreatic lipase activity by approximately 20% at a concentration of 100 µg/mL (Orlistat $IC_{50}$ of 0.8 µM) (vi).[154] *Cynara scolymus* L. appears as beneficial for metabolic syndrome.[155]

## 1.59 *Elephantopus mollis* Kunth

*Synonym*: *Elephantopus scaber* L.
*Common names*: di dan cao (Chinese); tutup bumi (Malay); malatabako (Philippines)
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: liver intoxication (Malaysia)

3,4-di-*O*-caffeoyl quinic acid isolated from the whole *Elephantopus mollis* Kunth inhibited α-glucosidase with an $IC_{50}$ value of 241.8 µg/mL (acarbose $IC_{50}$: 7.3 µg/mL).[156]

## 1.60 *Puchea indica* (L.) Less

*Synonyms*: *Baccharis indica* L.; *Erigeron denticulatum* Burm. f.
*Common names*: beluntas (Malay); luntas (Indonesia); tulo-lalaki (Philippines); Indian fleabane (India)
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: dysentery (Indonesia)

3,4,5-tri-*O*-caffeoylquinic acid methyl ester, 3,4,5-tri-*O*-caffeoylquinic acid, and 1,3,4,5-tetra-*O*-caffeoylquinic acid from the leaves of *Pluchea indica* (L.) Less. (Figure 1.38) inhibited rat-intestinal maltase with $IC_{50}$ values of 2, 13, and 11 µM, respectively.[157]

**FIGURE 1.38** *Pluchea indica* (L.) Less.



## 1.61 *Silybum marianum* (L.) Gaertn.

*Synonyms Carduus marianus* L.; *Carthamus maculatum* (Scop.) Lam. *Cirsium maculatum* Scop.
*Common name*: milk thistle
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: jaundice (India)

Ethanol extract from fruits of *Sylibum marianum* (L.) Gaertn. had no effect of bacterial α-glucosidase but inhibited porcine pancreatic lipase activity by approximately 30% at a concentration of 100 μg/mL (orlistat $IC_{50}$ of 0.8 μM).[158] Sylimarin (a fraction composed of flavonolignans, sylibin, silychristin, and silydianin) from this plant given at a dose of 200 mg to patients with type 2 diabetes 3 times per day before meals for 4 months reduced fasting glycemia from 188 to 133 mg/dL, and had no effect on plasma insulin.[159]

## 1.62 *Spilanthes acmella* (L.) L.

*Synonyms*: *Bidens acmella* (L.) Lam.; *Bidens ocymifolia* Lam.; *Pyrethrum acmella* (L.) Medik.; *Spilanthes ocymifolia* (Lam.) A.H. Moore; *Verbesina acmella* L.
*Common names*: hin ka la (Burmese); krishnarjaka (Sri Lanka); pokok getang kerbau (Malay); biri (Philippines); tooth ache plant

Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: diuretic (Sri Lanka)

Ethanol extract from flower buds of *Spilanthes acmella* (L.) L. at a concentration of 2 mg/mL inhibited human pancreatic lipase by about 44%.[160] This plant contains series of isobutylamides which comprise spilanthol as well as *trans*-ferulic acid, *trans*-isoferulic acid, and scopolelin.[161] It must be noted that the flowers contain *N*-isobutyl amides: spilanthol, undeca-2E,7Z,9E-trienoic acid isobutylamide, and undeca-2E-en-8,10-diynoic acid isobutylamide, which may account for pancreatic lipase inhibition.[162]

## 1.63 *Taraxacum officinale* F.H. Wigg.

*Synonyms*: *Leontodon taraxacum* L.
*Common names*: kanphool (Pakistan); dandelion
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: jaundice (Pakistan)

from leaves of *Taraxacum officinale* F.H. Wigg. inhibited porcine pancreatic lipase with an $IC_{50}$ value of 78.2 μg/mL, whereas orlistat had $IC_{50}$ value of 0.22 μg/mL.[163] The extract given orally at a single dose of 400 mg/kg to ICR mice challenged with oral administration of corn oil reduced postprandial plasma triglycerides from 76.9 mg/dL to about 60 mg/dL at 180 minutes.[163] Pancreatic lipase inhibition was confirmed by Villiger et al. (2015) who reported that ethanol extract of roots of *Taraxacum officinale* F.H. Wigg. inhibited porcine pancreatic lipase with an $IC_{50}$ value of 78.2 μg/mL (orlistat $IC_{50}$: 0.8 μM).[158] The plant shelters flavonoids which comprise of quercetin, luteolin, and luteolin-7-*O*-glucoside (chlorogenic acid, chicoric acid, and cichorin).[164,165] This plant may be of value for metabolic syndrome.

## 1.64 *Tussilago farfara* L.

*Common names*: kuan dong (Chinese); colt's-foot
Subclass Asteridae, Superorder Asteranae, Order Asterales, Family Asteraceae
*Medicinal use*: difficult breathing (China)

It must be recalled that such phenolics are common in members of the Family Asteraceae. *Tussilago farfara* L. elaborates series of caffeoylquinic derivatives that are able to inhibit carbohydrates and triglycerides absorption. 3,4-Dicaffeoylquinic acid, 3,5-dicaffeoylquinic acid, and 4,5-dicaffeoyllquinic acid isolated from the flower buds of *Tussilago farfara* L. inhibited rat-intestinal α-glucosidase *in vitro* with $IC_{50}$ values of 0.9, 0.9, and 0.8 mM, respectively, whereas cholorogenic acid was inactive.[166] At a concentration of 1 mM, 3,4-dicaffeoylquinic acid, 3,5-dicaffeoylquinic acid, and 4,5-dicaffeoylquinic acid inhibited rat-intestinal maltase by 65, 64, and 62%, respectively, *in vitro,* but these caffeic acid derivatives showed weak inhibitory activity against sucrase, isomaltase, and porcine pancreatic α-amylase.[166] From the same plant, rutin inhibited α-glucosidase by 41% at a concentration of 1 mM.[166] Positive standard 1,2,3,4,6-penta-*O*-galloyl-β-D-glucopyranose gave $IC_{50}$ value of 0.1 mM.[166] Park et al. (2008) provided evidence that tussilagone, 7β-(3-ethyl-cis-crotonoyloxy)-1α-(2-methylbutyryloxy)-3,14-dehydro-Z-notonipetranone and the bisabolane sesquiterpene 8-angeloyloxy-3,4-epoxy-bisabola-7(14),10-dien-2-one inhibited human diacylglycerol acyltransferase-1, which catalyze the formation of triglycerides from diacylglycerol in enterocytes, with $IC_{50}$ values of 49.1, 160.7, and 294.4 μM.[167] This plant should not be used in therapeutic strategies as it contains hepatotoxic pyrrolizidine alkaloids.[168]

## 1.65 *Gardenia jasminoides* J. Ellis

*Synonyms*: *Gardenia augusta* Merr.; *Gardenia florida* L.; *Varneria augusta* L.
*Common names*: zhi zi (Chinese); karinga (India); cape jasmine
Subclass Lamiidae, Superorder Lamianae, Order Rubiales, Family Rubiaceae
*Medicinal use*: jaundice (China)

Based on its ability to reduce the absorption of dietary triglycerides, orlistat (Xenical®, Roche) is used as an adjunct treatment of obesity in conjunction with mild diet restriction.[169] It is taken in adults at a dose of 120 mg before, during, or up to each main meal but has many side effects, hence the need to develop new leads.[169] The carotenoid glycoside crocin and its aglycone crocetin isolated from the fruits of *Gardenia jasminoides* J. Ellis (Figure 1.39) inhibited pancreatic lipase with $IC_{50}$ values of 2.7 and 2.1 mg/mL (orlistat: $IC_{50}$: 0.8 mg/mL).[170] Crocin and crocetin at doses of 50 mg/kg/day given orally to high-fat diet ICR mice for 5 weeks reduced triglycerides from 160.4 to 114.6 and 111.9 mg/dL (normal: 74.9 mg/dL; orlistat 10 mg/kg/day: 81.1 mg/dL); total cholesterol from 248 mg/dL to 170.5 mg/dL to 159.1 mg/dL (normal: 93.1 mg/dL; orlistat 10 mg/kg/day: 159.6 mg/dL).[170] This finding was confirmed by Sheng et al. (2006) who reported that crocin evoked 50% inhibition of pancreatic lipase at a concentration of 28.6 µmol/L *in vitro*. Crocin given orally to rats at single dose 100 mg/kg with a lipid emulsion reduced postprandial plasma

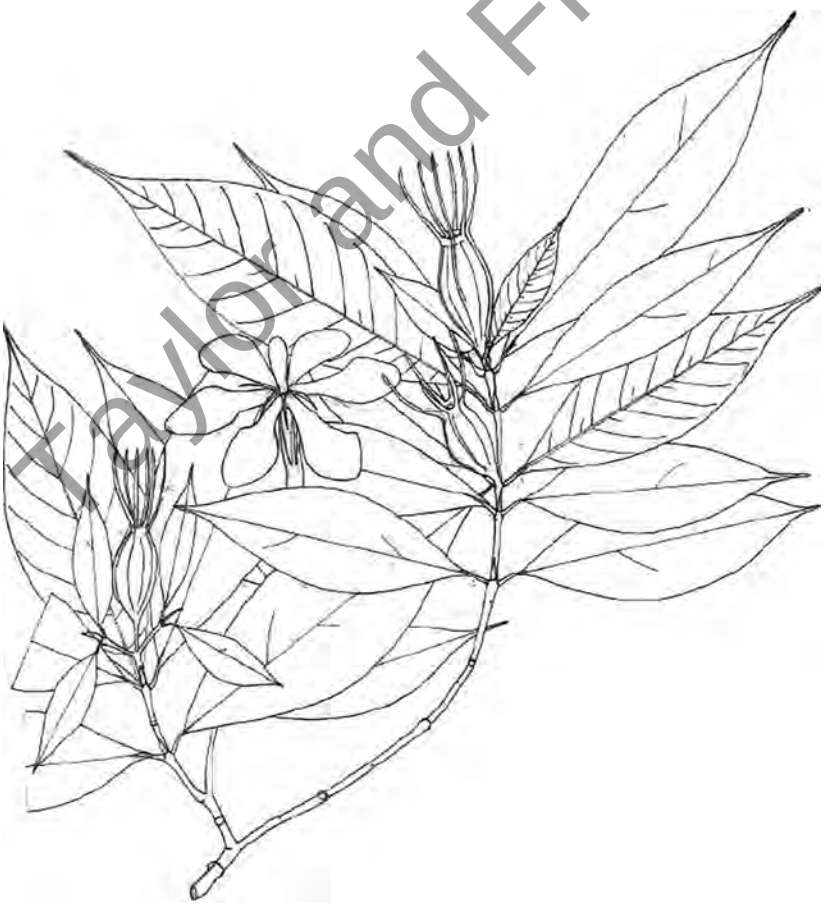


**FIGURE 1.39** *Gardenia jasminoides* J. Ellis.

triglycerides peak at 6 hours from about 250 to 75 mg/dL and plasma cholesterol peak at 9 hours from about 290 to 140 mg/dL, respectively.[171] In line, rats on high-fat diet given crocin orally at a dose of 100 mg/kg/day for 2 days had increased fecal secretion of cholesterol.[171] These experimental evidences lend support to the suggestion that the fruits of *Gardenia jasminoides* J. Ellis, if not toxic, could be of value for the treatment of metabolic syndrome.

## 1.66 *Uncaria laevigata* Wall. ex G. Don

*Synonym*: *Nauclea laevigata* (Wall. ex G. Don) Walp.
*Common name*: ping hua gou teng (Chinese)
Subclass Lamiidae, Superorder Lamianae, Order Rubiales, Family Rubiaceae
*Medicinal use*: hypertension (China)

Ursolic acid and 3β-hydroxy-30-methoxy-6-oxo-urs-12,19(20)-dien-28-oic acid isolated from the stem bark of *Uncaria laevigata* Wall. ex G. Don inhibited yeast α-glucosidase with $IC_{50}$ values of 16 and 49 μM, respectively.[172]

## 1.67 *Swertia kouitchensis* Franch.

*Synonym*: *Swertia elongata* T.N. Ho & S.W. Liu
*Common name*: gui zhou zhang ya cai (Chinese)
Subclass Lamiidae, Superorder Lamianeae, Order Rubiales, Family Gentianaceae
*Medicinal use*: diabetes (China)

The xanthones kouitchenside B, kouitchenside D, kouitchenside, and kouitchenside F isolated from *Swertia kouitchensis* Franch. inhibited yeast α-glucosidase with $IC_{50}$ values of 383, 360, 371, and 184 μM, respectively (acarbose: 627 μM).[173] Ethanol extract of *Swertia kouitchensis* inhibited porcine pancreas α-amylase and yeast α-glucosidase with $IC_{50}$ values of 0.1 and 0.9 mg/mL, respectively (acarbose: 0.04 and 0.7 mg/mL, respectively).[173] In oral starch tolerance test, a single oral dose of 500 mg/kg of extract decreased glucose area under the curve by 16.7% (acarbose: 23.4%). Ethanol extract given to high-fat and fructose diet-streptozotocin-induced diabetic Balb/c mice (fasting blood glucose superior or equal to 11.1 mmol/L) at a dose of 500 mg/kg/day reduced glycaemia from about 16 to 12 mmol/L (normal: 5 mmol/L; glicazide at 15 mg/kg/day: about 7 mmol/L).[174] This plant contains the iridoid swertiamarin (Figure 1.40) and its intestinal metabolite erythrocentaurin, inhibited the activity of α-amylase and α-glucosidase *in vitro* with $IC_{50}$ values of 0.1 and 10 mg/mL, respectively.[175]



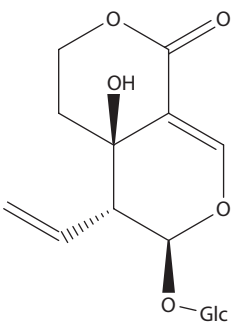



**FIGURE 1.40** Swertiamarin.

## 1.68 *Alstonia macrophylla* Wall. ex G. Don

*Common names*: da ye tang jiao shu (Chinese); batino (Philippines)
Subclass Lamiidae, Superorder Lamianeae, Order Rubiales, Family Apocynaceae
*Medicinal use*: dysmenorrhea (Philippines)

The indole alkaloids alstiphyllanines E and F inhibited $Na^+$ glucose cotransporter -1 (SGLT1) by 60.3% and 65.2%, respectively. From the same plant, 10-methoxy-N(1)-methylburnamine-17-*O*-veratrate alstiphyllanine D inhibited $Na^+$ glucose cotransporter -1 (SGLT1) by 95.8% and 89.9%, respectively.[176]

## 1.69 *Carissa carandas* L.

*Synonyms*: *Arduina carandas* (L.) K. Schum.; *Carissa congesta* Wight.
*Common names*: ci huang guo (Chinese); karonda (India); Bengal current
Subclass Lamiidae, Superorder Lamianeae, Order Rubiales, Family Apocynaceae
*Medicinal use*: thirst (India)

Ethanol extracts from leaves of *Carissa carandas* L. inhibited yeast α-glucosidase with an $IC_{50}$ value of 21.1 μg/mL, whereby an $IC_{50}$ value of 117.2 μg/mL for acarbose was recorded.[177] The plant contains series of triterpenes of which of betulinic acid, oleanolic acid, and ursolic acid, which are known inhibitors of α-glucosidase.[178]

## 1.70 *Gymnema sylvestre* (Retz.) R.Br. ex Schult.

*Synonyms*: *Gymnema affine* Decne. *Gymnema alterniflorum* (Lour.) Merr.; *Gymnema formosanum* Warb. *Periploca sylvestris* Retz.
*Common name*: gurmar (India)
Subclass Lamiidae, Superorder Lamianeae, Order Rubiales, Family Asclepiadaceae
*Medicinal use*: diabetes (India)
*History*: The plant was known of Sushruta or its antidiabetic properties

Saponin fraction of leaves of *Gymnema sylvestre* given to Wistar rats on high-fat diet for 8 weeks at a dose of 100 mg/kg/day reduced body weight from about 300 to 250 g (rats fed on normal chow: about 245 g).[179] This fraction decreased food intake from 23.7 g/day to 18.4 g (normal diet: 19.4 g) reduced plasma triglycerides, cholesterol, and decreased glycaemia.[179] *In vitro*, the fraction at inhibited dose dependently the release of oleic acid from triolein catalyzed by pancreatic lipase with a maximum activity at 400 mg/dL.[179] Methanol extracts from *Gymnema sylvestre* inhibited by 48% glucose uptake by sodium-dependent glucose transporter 1 (SGLT1) in *Xenopus laevis* oocytes.[179] From *Gymnema sylvestre*, gymnemic acid V and gymnemic acid XV inhibited SGLT1 activity with $IC_{50}$ values of 5.9 and 0.1 μM, respectively (phlorizin: 0.2 μM).[180] Baskaran et al. (1990) provided evidence of the usefulness of this plant for metabolic syndrome.[181]

## 1.71 *Holarrhena antidysenterica* (L.) Wall. ex A. DC.

*Common names*: kurchi (India); kurchi tree
Subclass Lamiidae, Superorder Lamianeae, Order Rubiales, Family Apocynaceae
*Medicinal use*: dysentery (India).
*History*: The plant was known of Sushruta

Methanol extract from seeds of *Holarrhena antidysenterica* (L.) Wall. ex A. DC. inhibited α-glucosidase of rats with an $IC_{50}$ value of 0.5 mg/mL.[182] The extract given orally at a single dose of 400 mg/kg to rats 30 minutes before oral load of starch reduced peak postprandial glycaemia at 1 hour from approximately 225 to 125 mg/dL (acarbose 3 mg/kg: approximately 125 mg/dL).[182]

## 1.72 *Ipomoea batatas* (L.) Lam.

*Synonyms*: *Batatas edulis* (Thunb.) Choisy; *Convolvulus batatas* L.; *Convolvulus edulis* Thunb.
*Common names*: mitha alu (India); ubi keledek (Malay); kamote (Philippines); man thet (Thai); sweet potato
Subclass Lamiidae, Superoder Lamianae, Order Solanales, Family Convolvulaceae
*Medicinal use*: diabetes (India)

Aqueous extract from peel of roots of *Ipomoea batatas* (L.) Lam. (Figure 1.41) given to obese Zucker rats orally at a dose of 100 mg/kg/day for 8 weeks decreased plasma insulin from about 753 to 384 μU/mL and attenuated of plasma glucose.[183] This regimen reduced plasma triglycerides, free fatty acids, and had no effect on cholesterol.[183] This extract improved glucose tolerance in oral glucose tolerance test at the end of the regimen.[183] In a subsequent study, *Ipomoea batatas* (L.) Lam.

**FIGURE 1.41** *Ipomoea batatas* (L.) Lam.

given to type 2 diabetic patients at a dose of 4 g/day for 3 months decreased, fasting blood glucose from 138.2 to 128.5 mg/dL, reduced total cholesterol from 248.7 to 214.6 mg/dL, and decreased plasma triglycerides.[184] This treatment decreased glucose 2 hours after oral glucose tolerance test from 181 to 162.8 mg/dL.[184] 48.3% of treated diabetic patients achieved a mean fasting blood glucose below the upper normal limit (126 mg/dL) after 3 months versus 7.7% in placebo group.[184] A single oral administration of anthocyanin fraction extracted from the tubers of *Ipomoea batatas* (L.) Lam. at a dose of 400 mg/kg to Sprague–Dawley rats 5 minutes before oral leading of maltose decreased 30 minutes peak glycaemia from 170.3 to 143.8 mg/dL and decreased serum insulin from 2.8 to 1.1 ng/mL.[185] The extract had no effect on sucrose postprandial glycaemia.[185] From this fraction the diacetylated anthocyanin YGM-6 given at a single oral administration of 100 mg/kg to Sprague–Dawley rats 5 minutes before oral loading of maltose reduced 30 minutes plasma glucose by 25%, whereby acarbose at 3 mg/dL evoked about 45% reduction of 30 minutes glycaemia peak.[185] In parallel this anthocyanin reduced serum insulin from 2.8 to 1.6 ng/mL.[185] YGM-6 had no effect on sucrose or glucose postprandial glycaemia.[185] The leaves of *Ipomoea batatas* (L.) Lam. contains 3,4,5-tricaffeoylquinic acid inhibited rat-intestinal maltase, rat-intestinal sucrase, and human saliva α-amylase with an $IC_{50}$ value of 24 μM (acarbose: 0.4 μM), 574 μM (acarbose: 1.2 μM), and 634 μM, respectively.[185]

## 1.73 *Ipomoea aquatica* Forssk.

*Common names*: weng cai (Chinese); kalambi (India); kangkong
Subclass Lamiidae, Superoder Lamianae, Order Solanales, Family Convolvulaceae
*Nutritional use*: food (Sri Lanka)

Evidence is accumulating in favor of a beneficial effect of *Ipomoea aquatica* Forssk. on postprandial glycemia. Aqueous decoction of the plant given orally to Wistar rats at a single oral dose of 3 g/kg, 30 minutes before oral load of glucose, lowered postprandial glycaemia by 33.6% after 120 minutes.[186] Stems and leaves of *Ipomoea aquatica* Forssk. given at a dose of 3.4 g/kg/day to streptozotocin-induced diabetic Wistar rats (blood glucose > 250 mg/dL) for 7 days reduced glycaemia by 48.6%.[187] Aqueous juice made with 100 g of stems and leaves given to type 2 diabetic patients 30 minutes before oral load of glucose decreased 2 hours peak glycaemia by 29.4%.[187] Sokeng et al. (2007) provided evidence that aqueous extract of leafy stem of *Ipomoea aquatica* Forssk. perfused at a single dose of 160 mg/kg to *ex vivo* preparation of rat intestines inhibited intestinal glucose by about 30%.[188] Clinical trials are warranted.

## 1.74 *Echium vulgare* L.

*Common names*: lan ji (Chinese); viper bugloss
Subclass Lamiidae, Superorder Lamianae, Order Boraginales, Family Boraginaceae
*Medicinal use*: fissures of hands (Turkey)
*History*: The plant was known to Paulus Aegineta (625–690 AD), Greek physician

Ethanol extract of *Echium vulgare* L. inhibited porcine α-amylase with an $IC_{50}$ value of 69.1 μg/mL (acarbose: $IC_{50}$ 50 μg/mL) and inhibited porcine pancreatic lipase by 41% at a concentration of 2.5 mg/mL (orlistat: $IC_{50}$ 18 μg/mL).[189] Methanol extract from leaves of *Echium vulgare* L. at a concentration of 2.5 mg/mL inhibited α-amylase activity by 71.7% and inhibited porcine pancreatic lipase activity by 92.4% *in vitro*.[96] The plant contains hepatotoxic pyrrolizidine alkaloids and is of no use in therapeutic strategies. This is often the case with members of the family

Boraginaceae. However, the seeds are enriched with polyunsaturated fatty acids, stearidonic acid, and γ-linolenic acid that given at 2g/100g diet to African green monkeys for 6 weeks improved glucose tolerance.[190] Plant oils rich in γ-linolenic acid have some beneficial effects on diabetic complications because in diabetic patients there is a defect in the desaturation steps in the metabolism of linoleic acid.[186] Oil-enriched γ-linolenic acid (4 g) plus 2.4 g of sardine oil given to hospitalized obese noninsulin-dependent diabetes for 4 weeks induced a reduction of urinary excression of 11-dehydro-thromboxane B2 by 32%.[189] Added at 6% of diet for 32 weeks to In F344/DuCrj rats oil-enriched γ-linolenic acid reduced the occurrence of ventricular tachycardia and inhibited the duration of ventricular tachycardia induced by experimental and acute coronary artery occlusion compared to rodents receiving sheep fat at 6% of diet.[189] This regimen afforded a complete protection against ventricular fibrillation in ischaemic state.[189] It must be recalled that this plant is poisonous owing to pyrrolizidine alkaloids and cannot be used itself in therapeutic strategies. Its seed oil, however, may have some beneficial effects on metabolic syndrome.

## 1.75 *Heliotropium zeylanicum* Lam.

*Synonym*: *Heliotropium linifolium* Lehm.
*Common name*: Hasthishundi (India)
Subclass Lamiidae, Superoder Lamianae, Order Boraginales, Family Boraginaceae
*Medicinal use*: inflammation (India)

Methanol fraction of *Heliotropium zeylanicum* given orally to streptozotocin-induced diabetic Wistar rats (plasma glucose > 225 mg/dL) at a daily dose of 300 mg/kg for 14 days prevented weight loss, decreased food and water intake closely to tolbutamide at a dose of 10 mg/kg/day.[192] This extract lowered glycaemia from 312 to 118.2 mg/dL (normal: 85.2 mg/dL; tolbutamide 10 mg/kg/day: 112.5 mg/dL), cholesterol from 148.1 to 116.7 mg/dL (normal: 100 mg/dL; tolbutamide 10 mg/kg/day: 105.5 mg/dL), and triglycerides from 185.6 to 146.9 mg (normal: 97.5 mg/dL; tolbutamide 10 mg/kg/day: 108.3 mg/dL).[192] This regimen decreased hepatic lipid peroxidation and increased hepatic glutathione to values close to normal group.[192] This extract also increased superoxide dismutase activities in the liver of treated diabetic rodents.[192] Schoental and Frayn (1976) administered the pyrrolizidine alkaloid heliotrine, which occurs in members of the genus *Heliotropium* L. to white weanling rats at a dose of 300 mg/kg orally observed increased plasma insulin levels owed to severe pancreatic insults.[193] Again, these alkaloids are toxic and of no use in therapeutic.

## 1.76 *Lithospermum erythrorhizon* Siebold & Zucc.

*Synonym*: *Lithospermum officinale* var. *erythrorhizon* (Siebold & Zucc.) Maxim.
*Common names*: zi cao (Chinese); murasaki (Japanese); Chinese groomwell
*Medicinal use*: wounds (Japan)

Members of the family Boraginaceae synthetize naphthoquinones that inhibit acyl-CoA:cholesterol acyltransferase an enzyme that reduces plasma lipid levels by inhibiting intestinal cholesterol absorption.[191] Such naphthoquinones are acetylshikonin (Figure 1.42), isobutyrylshikonin, and β-hydroxyisovalerylshikonin isolated from the roots of *Lithospermum erythorhizon* Siebold & Zucc. which inhibited human acyl-CoA:cholesterol acyltransferase with $IC_{50}$ values of 112.2, 57.5, and 169.8 μM, respectively.[194] Inhibition of acyl-CoA:cholesterol acyltransferase also prevents the progression of atherosclerotic lesions by inhibiting the accumulation of cholesteryl ester in macrophages.[195] Acetylshikonin and β-hydroxyisovalerylshikonin inhibited human acyl-CoA:cholesterol acyltransferase-1 with $IC_{50}$ values of 128.9 and 186.9 μM.[194]

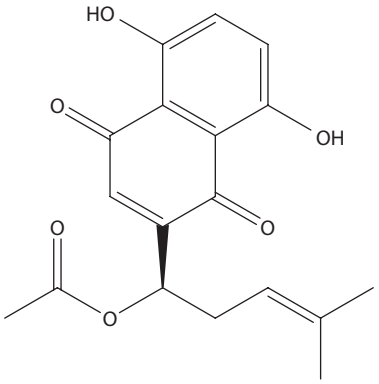



**FIGURE 1.42** Acetylshikonin.

## 1.77 *Olea europaea* L.

*Common name*: olive
Subclass Lamiidae, Superorder Lamianae, Order Oleales, Family Oleaceae
*Medicinal use*: nodules (Turkey)

Komaki et al. (2003) made the demonstration that aqueous extract from leaves of *Olea europea* L. could inhibit human pancreatic α-amylase activity *in vitro* with an $IC_{50}$ value of 70.2 mg/mL. From this extract, luteolin-7-*O*-β-glucoside and luteolin-4'-*O*-β-glucoside and oleanolic acid (Figure 1.43) inhibited human pancreatic α-amylase activity with $IC_{50}$ values of 0.5, 0.3, and 0.1 mg/mL.[196] In this experiment, luteolin inhibited human pancreatic α-amylase activity with $IC_{50}$ value of 0.01 mg/mL.[196] Oleanolic acid at 1 mg/kg or luteolin at 0.1 mg/kg given orally to type 2 diabetes Goto–Kakizaki/Jcl rats with starch decreased postprandial blood glucose levels from about 140 to 60 mg/dL after 120 minutes.[196] In healthy subject, the consumption of 1 g of leave powder with 300 g of cooked rice had no effect on postprandial glycemia, but given to borderline subject, leaf powder consumption reduced 1 hour peak glycemia evoked a decrease of postprandial glycemia from about 225 to 180 mg/dL at 1 hour.[196] In subsequent experiments, methanol

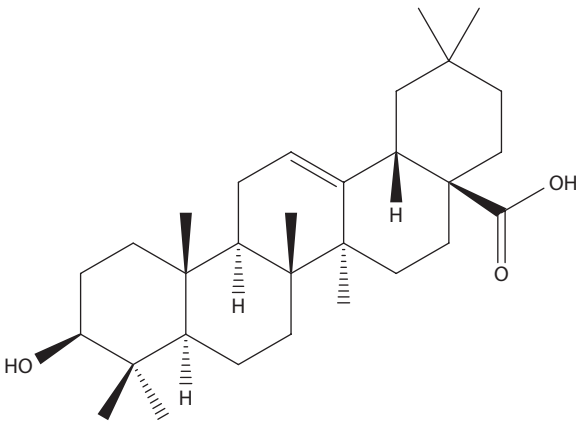



**FIGURE 1.43** Oleanolic acid.

extract of leaves at a concentration of 2.5 mg/mL inhibited α-amylase activity by 64.3% *in vitro* ($IC_{50}$: 0.8 mg/mL; acarbose: 1.3 μg/mL).[96] Methanol extract of leaves of *Olea europea* L. at a concentration of 2.5 mg/mL inhibited porcine pancreatic lipase activity by 100% *in vitro* ($IC_{50}$: 0.1 mg/mL; orlistat: 0.1 ng/mL).[96] In another study luteolin inhibited α-amylase with an $IC_{50}$ value of 18.4 μM.[15] If proven safe for consumption, the leaves of *Olea euroapea* L. could be used for metabolic syndrome.

## 1.78 *Dolichandrone falcata* Seem.

Subclass Lamiidae, Superorder Lamianae, Order Lamiales, Family Bignoniaceae
*Medicinal use*: body pain (India)

The phenylpropanoid glycoside dolichandroside A isolated from *Dolichandrone falcata* Seem. inhibited yeast and rat α-glucosidase with $IC_{50}$ values of 39.7 and 18.7 μg/mL, respectively.[197] From the same plant, 3,8-dihydroxy-1-methyl-9,10-anthraquinone inhibited yeast and rat α-glucosidase. Acarbose inhibited rat-intestinal α-glucosidase with an $IC_{50}$ value of 8.7 μg/mL.[197] Verbascoside was inactive in this study although being found active in other studies, exemplifying the variability of activities between rats and yeast α-glucosidase. Tadera et al. tested a series of flavonoids against yeast and rats α-glucosidase.[198] In yeast model, a concentration of 200 μM of kaempferol, naringenin, epigallocatechin, and cyanidin inhibited α-glucosidase activity by more than 70%.[198] The same flavonoids at a concentration of 0.5 mM were inactive and had no activity against rat-intestinal α-glucosidase suggesting that rat α-glucosidase should be prioritized for the testing of natural products.[198]

## 1.79 *Stereospermum colais* (Buch.-Ham ex Dillwyn) Mabb.

Subclass Lamiidae, Superorder Lamianae, Order Lamiales, Family Bignoniaceae
*Medicinal use*: In India, the roots are used to promote urination

Ursolic acid (Figure 1.44), lapachol, and pinoresinol isolated from the roots of *Stereospermum colais* (Buch.-Ham ex Dillwyn) Mabb. inhibited yeast α-glucosidase with $IC_{50}$ values of 12.4, 11, and 45.6 nM, respectively (acarbose $IC_{50}$: 55.6 nM).[199]

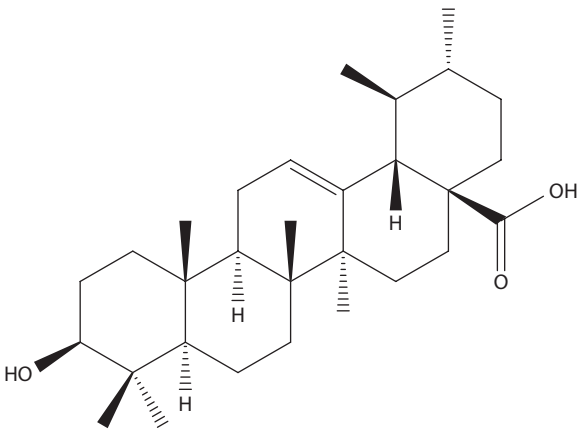



**FIGURE 1.44** Ursolic acid.

## 1.80 *Sesamum indicum* L.

*Synonym*: *Sesamum orientale* L.
*Common names*: zhi ma (Chinese); taila (India); sesame
Subclass Lamiidae, Superorder Lamianeae, Order Lamiales, Family Pedaliaceae
*Medicinal use*: ulcers (India)

The leaves of *Sesamum indicum* L. contains epigallocatechin inhibited α-amylase with an $IC_{50}$ value of 303.9 μM (acarbose: 124 μM).[200]

## 1.81 *Adhatoda vasica* Nees

*Synonym*: *Justicia adhatoda* L.
*Common names*: Sinha muki (India); Malabar nut tree
Subclass Lamiidae, Superoder Lamianae, Order Lamiales, Family Acanthaceae
*Medicinal use*: bronchitis (India)
*History*: The plant was known to Sushruta

Quinazoline alkaloids vasicine and vasicinone isolated from the leaves *Adhatoda vasica* Nees (Figure 1.45) inhibited rat sucrase by 93% and 81%, respectively, at a concentration of 1 mM.[201] Vasicine and vasicinone inhibited rat maltase by about 32% and 29%, and inhibited pancreatic α-amylase by about 12% and 19%.[201]



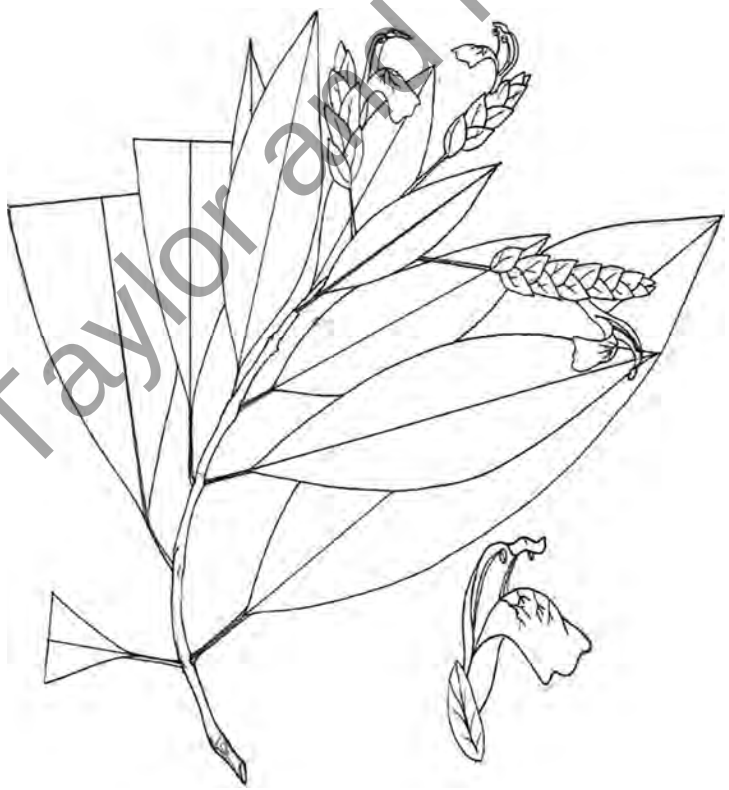


**FIGURE 1.45** *Adhatoda vasica* Nees.

## 1.82 *Clerodendrum bungei* Steud.

*Synonym*: *Clerodendrum foetidum* Bunge
*Common name*: xiu mu dan (Chinese)
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
*Medicinal use*: hypertension (China)

Verbascoside, leucosceptoside, and isoacteoside isolated from the roots of *Clerodendrum bungei* Steud. inhibited yeast α-glucosidase with $IC_{50}$ values of 0.5, 0.7, and 0.1 mM, respectively (acarbose $IC_{50}$: 14.4 mM).[202]

## 1.83 *Duranta repens* L.

*Synonym*: *Duranta erecta* L.
*Common name*: golden dewdrop
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Verbenaceae
*Medicinal use*: dysmenorrhea (Indonesia)

7-*O*-α-D-glucopyranosyl-3,5-dihydroxy-3′-(4″-acetoxyl-3″-methylbutyl)-6,4′-dimethoxyflavone, 3,7,4′-trihydroxy-3′-(8″acetoxy-7″-methyloctyl)-5,6-dimethoxyflavone and (–)-6β-hydroxy-5β, 8β, 9β, 10α-cleroda-3,13-dien-16,15-olid-18-oic acid isolated from *Duranta repens* inhibited yeast α-glucosidase with $IC_{50}$ values of 65.5, 757.8, and 577.7 μg/mL (deoxynojirimycin $IC_{50}$: 425.6 μg/mL).[203] The plant is poisonous.

## 1.84 *Premna tomentosa* Kurz

*Common name*: bastard teak
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Verbenaceae
*Medicinal use*: liver disorder (India)

8,11,13-Icetexatriene-10-hydroxy-11,12,16-tri acetoxyl, 8,11,13-icetexatriene-7,10,11-dihydroxy-12,13-dihydrofuran and acetoxy syringaldehyde isolated from the roots of *Premna tomentosa* inhibited rat-intestinal α-glucosidase with $IC_{50}$ values of 22.5, 9.5, and 18.4 μg/mL, respectively.[204]

## 1.85 *Tectona grandis* L.f.

*Synonyms*: *Tectona theka* Lour.; *Theka grandis* (L.f.) Lam.
*Common names*: you mu (Chinese); malapangit (Philippines); teak
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Verbenaceae
*Medicinal use*: sore throat (Philippines)

Methanol extract from flowers of *Tectona grandis* L.f. given to nicotinamide-streptozotocin-induced type 2 diabetic Wistar albino rats (glycaemia > 200 mg/dL) at a dose of 200 mg/kg/day orally for 4 weeks prevented weight loss and decreased glycaemia to about 100 mg/dL.[205] This extract inhibited α-amylase with an $IC_{50}$ value of 2.2 μg/mL (acarbose: 219.5 μg/mL) and α-glucosidase with an $IC_{50}$ value of 229.2 μg/mL (acarbose: 0.3 μg/mL).[205] The flowers shelter phenolic constituents including ellagic acid, quercetin, and rutin that are known inhibitors of α-glucosidase *in vitro*.[205] Quercetin inhibited α-amylase activity with an $IC_{50}$ value of 21.4 μM.[15]

## 1.86 *Calamintha officinalis* Moench

*Synonyms*: *Calamintha nepeta* (L.) Savi; *Melissa calamintha* L.
*Common name*: calamint
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
Nutritional use: seasoning (Turkey)

In healthy individual, plasma glucose levels reach a peak not exceeding 160 mg/dL from 30 to 60 minutes after oral ingestion of 75 g of glucose and gradually return to postabsorptive values by 3–4 hours and insulin resistance in metabolic syndrome elevates that peak, posing the threat of toxic plasma levels of glucose also called "glucotoxicity".[64] *Calamintha officinalis* Moench given orally to alloxan-induced diabetic Wistar rats orally at a dose of 400 mg/kg/day for 14 days decreased plasma glucose from 248.6 to 117.7 mg/dL.[206] Rosmarinic acid (Figure 1.46) or caffeic acid isolated from this extract given orally at a dose of 10 mg/kg/day to alloxan-induced diabetic Wistar rats decreased glycaemia from 248.6 to 97.3 mg/dL and 105.4 mg/dL, respectively, whereby glibenclamide at 10 mg/kg brought glycaemia down to 115.1 mg/dL (normal: 87.5 mg/dL).[207] From the extract, rosmarinic acid and caffeic acid decreased triglycerides and normalized plasma cholesterol.[207] Caffeic acid which is common in members of the family Lamiaceae inhibited yeast α-glucosidase with $IC_{50}$ values of 27.4 μM, respectively (acarbose: and 38.3 μM).[208] Rosmarinic acid common in this family inhibits α-glucosidase *in vitro*.[209]

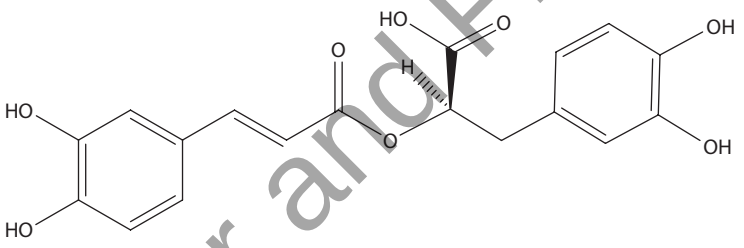



**FIGURE 1.46** Rosmarinic acid.

## 1.87 *Hyssopus officinalis* L.

*Synonym*: *Thymus hyssopus* (L.) E.H.L. Krause
*Common names*: shen xiang cao (Chinese); jupha (India); hyssop
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
*Medicinal use*: indigestion (India)
*History*: The plant was known of Pliny the Elder (23–79 AD). Roman scholar

The phenolic glycosides (7S,8S)-syringoylglycerol-9-*O*-(6′-*O*-cinnamoyl)-β-D-glucopyranoside and (7S,8S)-syringoylglycerol-9-*O*-β-D-glucopyranoside from *Hyssopus officinalis* L. inhibited the enzymatic activity of rat-intestinal α-glucosidase by 54% and 53% at a concentration of $3 \times 10^{-3}$ M.[209]

## 1.88 *Melissa officinalis* L.

*Synonym*: *Melissa bicornis* Klokov
*Common names*: xiang feng hua (Chinese); lemon balm
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae

*Medicinal use*: arteriosclerosis (Turkey)
*History*: The plant was known of Dioscarides as an antidote for snake bites.

Methanol extract from leaves of *Melissa officinalis* L. at a concentration of 2.5 mg/mL inhibited porcine pancreatic lipase activity by 90% *in vitro*.[96] The active constituents involved in pancreatic lipase inhibition are apparently unknown and would be worth being isolated. A pharmacologic inhibition of the absorption of triglycerides has been used as a clinical strategy in the treatment of obesity.[46] Such inhibitor is orlistat that inhibited porcine lipase with an $IC_{50}$ value of 0.2 mg/mL (Liu et al. 2013).[16] *Melissa officinalis* L. could be beneficial for metabolic syndrome management and further clinical studies in this direction are needed.

## 1.89 *Ocimum basilicum* L.

*Synonym*: *Ocimum thyrsiflorum* L.
*Common name*: luo le (China); kali tulasi (India); basil
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
*Medicinal use*: diuretic (India)

After a meal, postprandial glycaemia usually do not exceed 165 mg/dL but that value is increased in case of insulin resistance.[210] Inhibitors of amylase decrease postprandial glycemia.[211] Aqueous extract from leaves of *Ocimum basilicum* L. inhibited rat-intestinal amylase, rat-intestinal maltase, and porcine pancreatic amylase with $IC_{50}$ values of 36.7, 21.3, and 42.5 mg/mL (acarbose $IC_{50}$ of 0.03 μg/mL).[212]

## 1.90 *Origanum majorana* L.

*Synonyms*: *Majorana vulgaris* (L.) Gray; *Thymus majorana* (L.) Kuntze
*Common name*: sweet marjoram
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
*Nutritional use*: seasoning (Turkey)

*Origanum majorana* L. elaborates the monoterpene carvacrol (Figure 1.47) which inhibited lipase of ddY mice isolated from mice plasma with an $IC_{50}$ value of 4 mM (orlistat 0.09 mM).[213,214] Carvacrol given orally at a single dose of 300 mg/kg to ddY mice oral olive-oil load decreased, after 180 mon, blood triglycerides from about 900 to 300 mg/dL and this effect was comparable with orlistat at 10 mg/kg.[214] Scutellarein (or 6-hydroxyluteolin) and 6-hydroxyluteolin-7-*O*-β-D-glucopyranoside isolated from *Origanum marjorana* inhibited rat-intestinal α-glucosidase with an $IC_{50}$ values of 12 and 300 μM, respectively.[215] In the same experiment, the isoflavones, flavanols, and flavanones tested had no activity. Scutellarein inhibited α-amylase *in vitro* with an $IC_{50}$ value of 9.6 μM.[15]

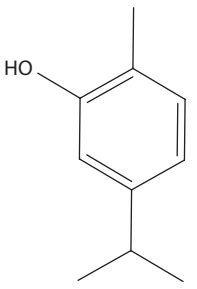



**FIGURE 1.47** Carvacrol.

## 1.91 *Orthosiphon stamineus* Benth.

*Synonyms*: *Clerodendranthus spicatus* (Thunb.) C.Y. Wu ex H.W. Li; *Orthosiphon aristatus* (Blume) Miq.
*Common names*: misai kunching (Malay); Java tea
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
*Medicinal use*: diuretic (Malaysia)

Tetramethylscutellarein and 3,7,4′-tri-O-methylkaempferol isolated from this plant inhibited yeast α-glucosidase with $IC_{50}$ values of 6.3 and 0.7 μM, respectively.[216] From this plant, orthosiphol A selectively inhibited intestinal maltase with an $IC_{50}$ value of 6.5 μM.[216]

## 1.92 *Rosmarinus officinalis* L.

*Common names*: mi die xiang (Chinese); romero (Philippines); rosemary
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
*Medicinal use*: tonic (Philippines)

Ninomiya et al. (2004) provided evidence that carnosic acid and carnosol from *Rosmarinus officinalis* L. inhibited porcine pancreatic lipase *in vitro* with $IC_{50}$ values of 12 and 4.4 μg/mL, respectively.[217] Methanol extract from the leaves at a concentration of 2.5 mg/mL inhibited porcine pancreatic lipase activity by 100% *in vitro* ($IC_{50}$: 0.1 mg/mL; orlistat: 0.1 ng/mL).[96] A fraction of *Rosmarinus officinalis* containing 38.9% carnosic acid given to obese Zucker rats orally as part of diet at 0.5% for 64 days did not reduce food consumption and evoked a mild reduction of body weight and increased fecal weight.[218] This supplementation reduced plasma triglycerides and had no effect on plasma cholesterol and glycemia or glycaemia.[218] The fraction inhibited gastric lipase activity by about 80% and had a mild effect on intestinal pancreatic lipase activity.[218] In a subsequent study, a fraction extracted from *Rosmarinus officinalis* L. containing 80% carnosic acid added to high-fat diet at 0.2% given to C57BL/6L for 16 weeks reduced body weight from about 50 to 35 g (normal diet: about 32.5 g), normalized liver mass, increased epididymal fat, reduced mesenteric fats, reduced retroperitoneal fat, and decreased total fat from 4.8 to 3.4 g (normal diet: 2.1 g).[219] This supplementation prevented rise in fasting glycaemia, decreased plasma insulin by 90% and insulin resistance by 96.4%, bringing both parameters to normal diet group.[219] This fraction reduced liver triglycerides by 109.4%, and free fatty acids by 106.7%.[219] The regimen attenuated enlargement and vacuolization of hepatocytes (steatosis).[219] The fraction decreased lipoperoxidation in the plasma and liver.[219] This fraction increased lipid fecal secretion implying, at least, inhibition of triglyceride absorption confirming pancreatic inhibition.[219] The plant contains rosmarinic acid and inhibits α-glucosidase *in vitro*.[208]

## 1.93 *Salvia miltiorrhiza* Bunge

*Common name*: dan shen (Chinese)
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
*Medicinal use* heart diseases (China)

Isosalvianolic acid C methyl ester, tanshinone IIA, rosmarinate acid, rosmarinic acid methyl ester, salvianolic acid A methyl ester, salvianolic acid C methyl ester isolated from *Salvia miltiorrhiza*

Bunge inhibited α-glucosidase activity with $IC_{50}$ value of $111.9 \times 10^{-3}$ μM, $230.2 \times 10^{-3}$ μM, $224.1 \times 10^{-3}$ μM, $142.6 \times 10^{-3}$ μM, $180.6 \times 10^{-3}$ μM, and $42.1 \times 10^{-3}$ μM, respectively (acarbose: $IC_{50}$ of $5832.4 \times 10^{-3}$ μM).[220]

## 1.94 *Salvia officinalis* L.

*Common names*: sa er wei ya (Chinese); Salbia sefakuss (India); sage
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
*Medicinal use*: indigestion (India)

Ethanol extract from leaves of *Salvia officinalis* L. given orally to type 2 diabetic patients at a dose of 500 mg 3 times per day for 3 months decreased fasting plasma glucose by 25.8%, total cholesterol by 17.7%, triglycerides by 32.2%, low density lipoprotein-cholesterol by 19.2%, and increased high-density lipoprotein-cholesterol by 34.8%.[221] Carnosic acid, carnosol, royleanonic acid, 7-methoxyrosmanol, and oleanolic acid isolated from *Salvia officinalis* L. inhibited porcine pancreatic lipase with $IC_{50}$ values below 85 μg/mL.[222] In ddY mice, carnosic acid at a single oral dose of 20 mg/kg 30 minutes before oral loading of olive oil, reduced 2 hours serum triglycerides from 571 to 220 mg/100 mL (orlistat: 177 mg/100 mL) whereby carnosol, royleanonic acid, 7-methoxyrosmanol, and oleanolic acid up to 200 mg/kg had no effect.[222] Carnosic acid given orally at a dose of 10 mg/kg/day for 14 days to ddY mice on high-fat diet, had no effect on body weight, decreased serum triglycerides from 126 to 78 mg/100 mL (normal: 118 mg/100 mL) and decreased epididymal fat pad from 1472 mg/mouse to 1018 mg/mouse (normal: 839 mg/mouse).[222] The consumption of sage tea could be beneficial in metabolic syndrome.

## 1.95 *Scutellaria baicalensis* Georgi

*Synonyms*: *Scutellaria lanceolaria* Miq.; *Scutellaria macrantha* Fisch.
*Common name*: huang qin (Chinese)
Subclass Lamiidae, Superorder Lamiidae, Order Lamiales, Family Lamiaceae
*Medicinal use*: fever (China)

Members of the genus *Scutellaria* L. synthetizes a broad array of flavones glycosides, of which luteolin 7-*O*-glucoside, luteolin 7-*O*-glucuronide, and diosmetin 7-*O*-glucuronide which inhibited *in vitro* porcine α-amylase with $IC_{50}$ values of 81.7, 61.5, and 76.3 μM, respectively (acarbose $IC_{50}$: 43.4 μM).[223] Luteolin 7-*O*-glucoside, luteolin 7-*O*-glucuronide, and diosmetin 7-*O*-glucuronide inhibited *in vitro* yeast α-glucosidase with $IC_{50}$ values of 18.3, 14.7, and 17.1 μM, respectively (acarbose $IC_{50}$: 16.1 μM).[223] *Scutellaria baicalensis* Georgi shelters baicalein that inhibited rat-intestinal sucrase with an $IC_{50}$ value of $3.5 \times 10^{-5}$ M.[224] Aqueous extract from roots of *Scutellaria baicalensis* Georgi at 18 mg/tube inhibited pancreatic lipase by 66%.[225]

## 1.96 *Chlorophytum borivilianum* Santapau & R.R. Fern.

*Common name*: shweta Musali (India)
Subclass Lillidae, Superorder Lilianae, Order Asparagales, Family Asparagaceae
*Medicinal use*: sex impotance (India)

Root powder of *Chlorophytum borivilianum* Santapau & R.R. Fern. given to Wistar rats on high-fat diet at a dose of 1.5 g/rat/day for 4 weeks decreased plasma cholesterol from 363.1 to 265 mg/dL

(normal: 119.9 mg/dL) and triglycerides from 55.9 to 44.7 mg/dL (normal: 43.5 mg/dL).[226] At the hepatic level, the supplementation decreased cholesterol, triglycerides, 3-hydroxy-3-methylglutaryl-coenzyme A reductase activity, and increased bile acids from 6.5 to 8.7 mg/g.[226] The root powder increased fecal cholesterol, neutral fecal sterol, and fecal bile acids suggesting a decrease of intestinal cholesterol absorption. Root powder of *Chlorophytum borivilianum* Santapau & R.R. Fern. contains inulin-type fructans and saponins.[227] In rats, a decrease in plasma triglycerides and cholesterol have been reported after oral administration of fructans.[150,151]

## 1.97 *Dendrobium loddigesii* Rolfe

*Synonyms*: *Callista loddigesii* (Rolfe) Kuntze
*Common name*: mei hua shi hu (China)
Subclass Liliidae, Superorder Lilianae, Order Orchidales, Family Orchidaceae
*Medicinal use*: indigestion (China)

Loddigesiinol G, H, I, J, and crepidatuol B isolated from the stems of *Dendrobium loddigesii* inhibited α-glucosidase with $IC_{50}$ values below 20 μM (trans-resveratrol: 27.9 μM).[228]

## 1.98 *Dioscorea bulbifera* L.

*Synonyms*: *Dioscorea sativa* Thunb.; *Helmia bulbifera* (L.) Kunth
*Common names*: huang du (Chinese); eeloom poom paw (Thai); potato yam
Subclass Liliidae, Superorder Dioscoreanae, Order Dioscoreales, Family Dioscoreaceae
*Medicinal use*: boils (China)

Diosgenin (Figure 1.48) isolated from the bulbs of *Dioscorea bulbifera* L. at a concentration of 100 μg/mL inhibited porcine pancreatic α-amylase by 70.9%, crude murine pancreatic α–amylase by 39.5%, and yeast α-glucosidase by 81.7%, and crude murine intestinal α-glucosidase by 70.7%.[229] It would be of interest to assess the activity of this plant on pancreatic lipase as 3,3′,5-trihydroxy-2′-methoxybibenzyl isolated from another member of the genus *Dioscorea* inhibited lipase with an $IC_{50}$ value of 8.8 μM.[230]



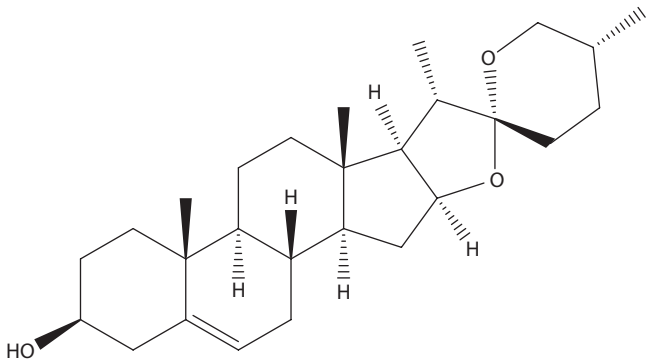



**FIGURE 1.48** Diosgenin.

## 1.99 *Alpinia officinarum* Hance

*Synonym*: *Languas officinarum* (Hance) Farw.
*Common names*: gao liang jiang (Chinese); galangal
Subclass Commelinidae, Superoder Zingiberanae, Order Zingiberales, Family Zingiberaceae
*Medicinal use*: indigestion (China)
*History*: The plant was known of Avicenna

Shin et al. (2003) provided evidence that 3-methylethergalangin (Figure 1.49) isolated from the rhizome of *Alpinia officinarum* Hance (Figure 1.50) inhibited pancreatic lipase activity with an $IC_{50}$

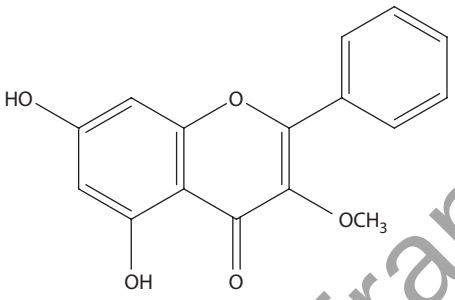



**FIGURE 1.49** 3-Methylethergalangin.

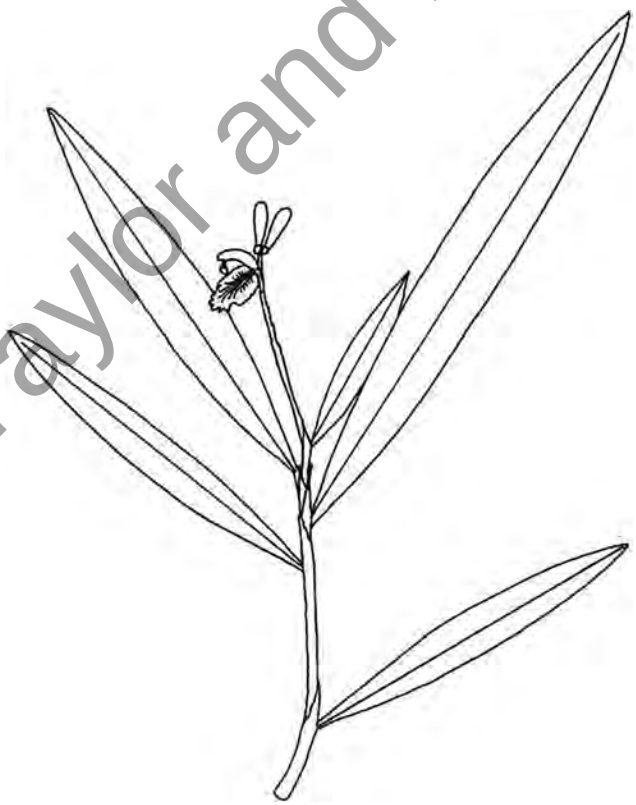


**FIGURE 1.50** *Alpinia officinarum* Hance.

value of 1.3 mg/mL (orlistat, $IC_{50}$: 0.8 mg/mL).[231] This flavone given orally at a dose of 20 mg/kg/day to corn oil induced hyperlipidemic ICR mice for 5 days decreased triglycerides from 88 to 39.3 mg/dL (normal: 48.1 mg/dL; orlistat 20 mg/kg/day: 31.5 mg/dL) and increased cholesterol from 167.5 to 182.9 mg/dL (normal: 175 mg/dL; orlistat 20 mg/kg/day: 172.2 mg/dL).[231] From the same plant, 5-hydroxy-7-(4'-hydroxy-3'-methoxyphenyl)-1-phenyl-3-heptanone inhibited pancreatic lipase activity with an $IC_{50}$ value of 1.5 mg/mL (orlistat, $IC_{50}$: 0.8 mg/mL).[232] This curcumoid given orally at a dose of 100 mg/kg/day to corn oil induced hyperlipidemic ICR mice for 5 days decreased triglycerides from 188 to 116.8 mg/dL (normal: 97.3 mg/dL; orlistat 50 mg/kg/day: 63.9 mg/dL), cholesterol from 137.5 to 112.6 mg/dL (normal: 123.3 mg/dL; orlistat 50 mg/kg/day: 126.4 mg/dL), and had no effect on high-density lipoprotein.[232] Rhizomes of *Alpinia officinarum* Hance given to Syrian hamsters at 10% of high-fat diet for 9 weeks attenuated food intake, reduced weight gain from 44 to 34.6 g (normal diet: 35 g), prevented liver weight gain, decreased serum cholesterol from 319 to 116 mg/dL (normal: 138 mg/dL), triglycerides from 223 to 94 mg/dL (normal: 98 mg/dL), low-density lipoprotein cholesterol from 108 to 40 mg/dL (normal: 40 mg/dL), and lowered high-density lipoprotein cholesterol from 194 to 167 mg/dL (normal: 168 mg/dL).[233] This supplementation increased serum superoxide dismutase, decreased catalase, decreased serum lipid peroxides, and increased glutathione.[233] Increase of high-density lipoprotein-cholesterol by 10 mg/dL in human corresponds to a 19% decrease in coronary artery disease death.[234] Clinical trials are warranted.

## 1.100 *Curcuma longa* L.

*Synonym*: *Curcuma domestica* Valeton
*Common names*: jiang huang (Chinese); dilau (Philippines); turmeric
Subclass Commelinidae, Superoder Zingiberanae, Order Zingiberales, Family Zingiberaceae
*Medicinal use*: diabetes (Philippines)

Curcumin (Figure 1.51), demethoxycurcumin, and bisdemethoxycurcumin, which are not absorbed in the small intestine, isolated from the rhizomes of *Curcuma longa* L. inhibited yeast α-glucosidase with $IC_{50}$ values of 37.2, 42.7, and 23 mM, respectively.[235]

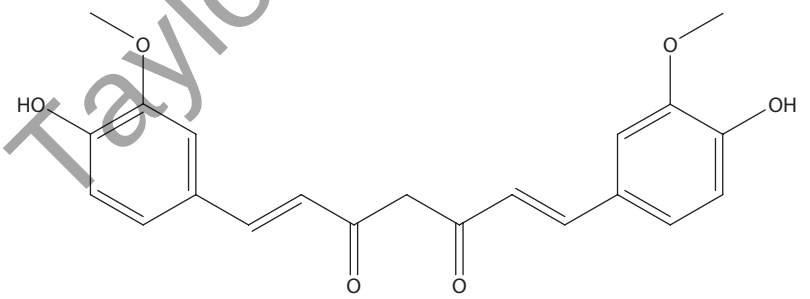



**FIGURE 1.51** Curcumin.

## 1.101 *Hedychium spicatum* Buch.-Ham. ex Sm.

*Synonyms*: *Hedychium Coronarium* J. Koenig
*Common name*: cao guo yao (Chinese)
Subclass Commelinidae, Superoder Zingiberanae, Order Zingiberales, Family Zingiberaceae
*Medicinal use*: indigestion (Taiwan)

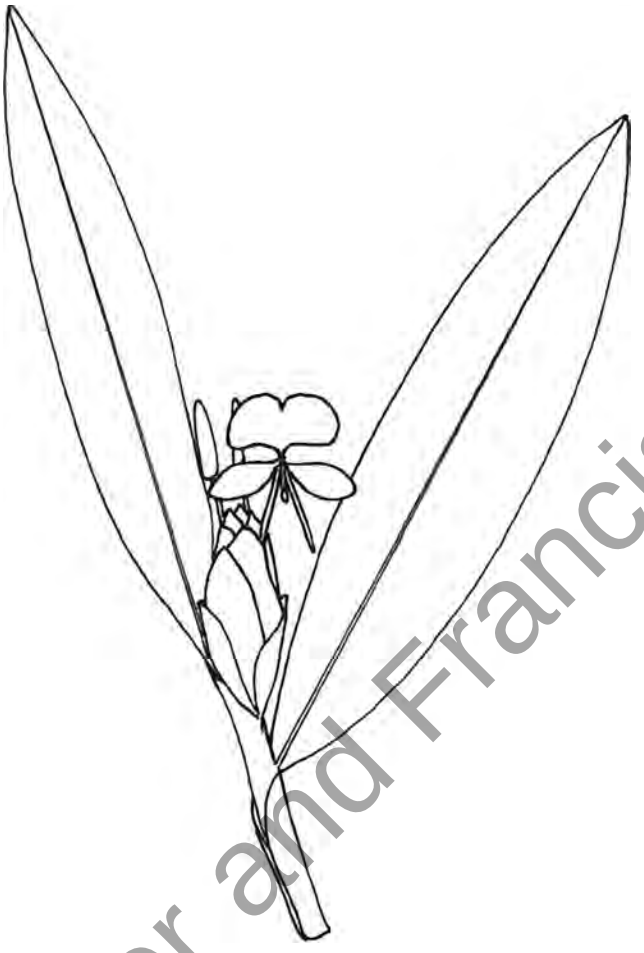


**FIGURE 1.52** *Hedychium spicatum* Buch.-Ham. ex Sm.



Spicatanol methyl ether and hedychenone isolated from the rhizome of *Hedychium spicatum* Buch.-Ham. ex Sm. (Figure 1.52) at a concentration of 100 μg/mL inhibited rat-intestinal α-glucosidase by more than 50%.[236] Spicatanol inhibited rat-intestinal α-glucosidase with an $IC_{50}$ value of 34.1 μM (acarbose: $IC_{50}$ of 23.8 μM).[236]

## 1.102 *Kaempferia parviflora* Wall. ex Baker

*Synonyms*: *Kaempferia rubromarginata* (S.Q. Tong) R. J. Searle; *Stahlianthus rubromarginatus* S.Q. Tong
*Common name*: kalahalood (Bangladesh)
Subclass Commelinidae, Superoder Zingiberanae, Order Zingiberales, Family Zingiberaceae
*Medicinal use*: diarrhea (India)

Methoxyflavones fraction of rhizome of *Kaempferia parviflora* Wall. ex Baker given to Tsumara Suzuki Obese Diabetes (TSOD) mice at 1% of diet for 8 weeks had no effect on food intake, evoked a decrease in body weight gain and visceral fat mass.[237] The fraction lowered glycemia from 216 to 152 mg/dL (normal mice: 152 mg/dL), it had no effect on cholesterol and triglycerides and

evoked a decrease in plasma insulin from 15.6 to 5.9 ng/mL (normal mice: 1.1 ng/mL).[237] In oral glucose tolerance test performed at the end of the treatment, the extract reduced 30 minutes peak postprandial glycemia from about 500 to 325 mg/dL. The extract reduced hepatic cholesterol and triglycerides from 14.1 to 8.1 mg and 1.8 to 1.3 mg.[237] The systolic blood pressure was reduced from 112.9 to 102.3 mmHg (i). In a parallel study, powder of rhizome of *Kaempferia parvifolia* given to Tsumara Suzuki Obese Diabetes (TSOD) mice for 8 weeks at 3% of diet had no effect on food intake, decreased body weight gain, and reduced visceral fat accumulation (not subcutaneous).[238] This regimen reduced plasma glucose from 184 to 159 mg/dL, plasma cholesterol from 228 to 172 mg/dL, triglycerides from 234 to 166 mg/dL, it had no effect on low-density lipoprotein, reduced high-density lipoprotein from 123 to 104 mg/dL, and decreased insulin from 10.3 to 2.9 ng/mL.[238] In line, the treatment reduced 30 minutes postprandial peak glycemia in oral glucose tolerance test from about 650 to 500 mg/dL.[238] From the extract, 5-hydroxy-3,7-dimethoxyflavone, 5-hydroxy-3,7,4'-trimethoxyflavone, 5-hydroxy-7.4'-dimethoxyflavone, and 5-hydroxy-7-methoxyflavone inhibited porcine pancreatic lipase with $IC_{50}$ values below 550 μg/mL.[238]

## 1.103 *Commelina communis* L.

*Synonym*: *Commelina coreana* H. Lév.; *Commelina ludens* Miq.
*Common name*: ya zhi cao (Chinese)
Subclass Commelinidae Superorder Commelinanae, Order Commelinales, Family Commelinaceae
*Medicinal use*: fever (China)

Kim et al. (1999) isolated from *Commelina communis* L. the polyhydroxylated piperidine alkaloids, 1-deoxymannojirimycin, 1-deoxynojirimycin, and α-homonojirimycin.[239] Aqueous extracts from leaves of *Commelina communis* L. and whole plant at a dose of 10 mg/mL inhibited the enzymatic activity of α-glucosidase by 77% and 62.1%, respectively.[239] Administration of extract at a dose of 100 mg/kg for 10 days evoked a mild reduction of fasting blood glucose. In healthy mice, the leaf extract at a dose of 100 mg/kg halved the postprandial hyperglycemia caused by starch loading at 2 g/kg.[240] 1-Deoxynojirimycin (Figure 1.53), which is produced by both *Streptomyces* and flowering plants from various taxons (symbionts?), is a glucose analogue with an amine group substituting for the oxygen atom in the pyranose ring, has been shown to inhibit intestinal α-glucosidases and pancreatic α-amylase both *in vitro* and *in vivo*. This molecule has been used for the development of miglitol, a drug given to lower postprandial glycemia in type 2 diabetes.[241] 1-Deoxynojirimycin inhibits rat-intestinal maltase and isomaltase with $IC_{50}$ of 0.3 mM whereas, 1-deoxymannojirimycin inhibits rat intestine maltase with $IC_{50}$ of 150 mM.[241] As for α-homonojirimycin, it is known to inhibit α-glucosidase.[242] Insulin resistance is associated with hyperglycaemia, a risk factor for cardiovascular disease and this plant, if not toxic, may be of value in metabolic syndrome.[243]

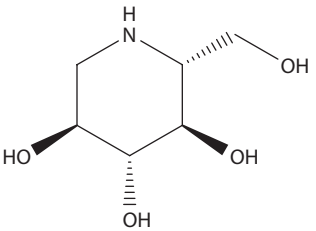
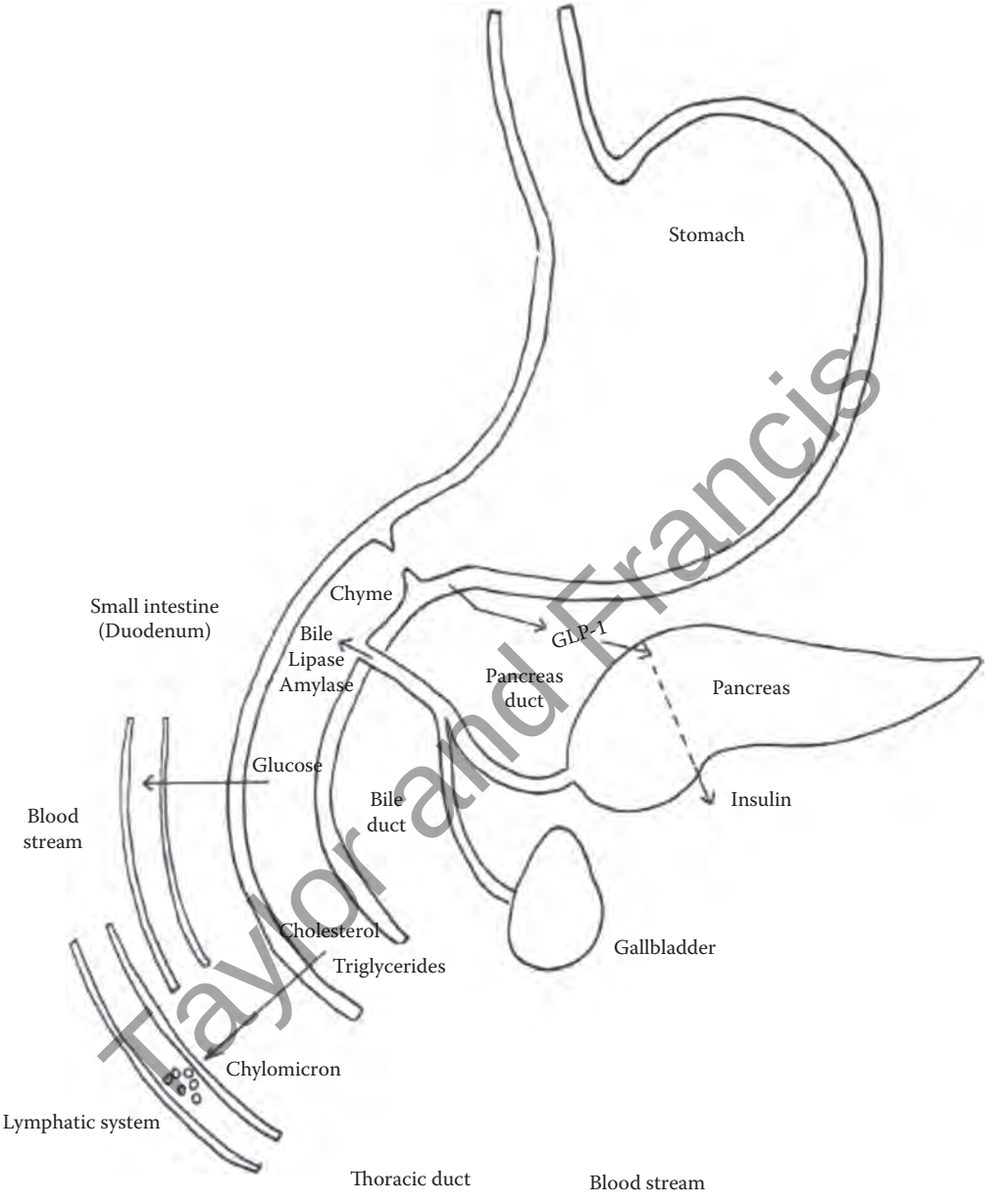
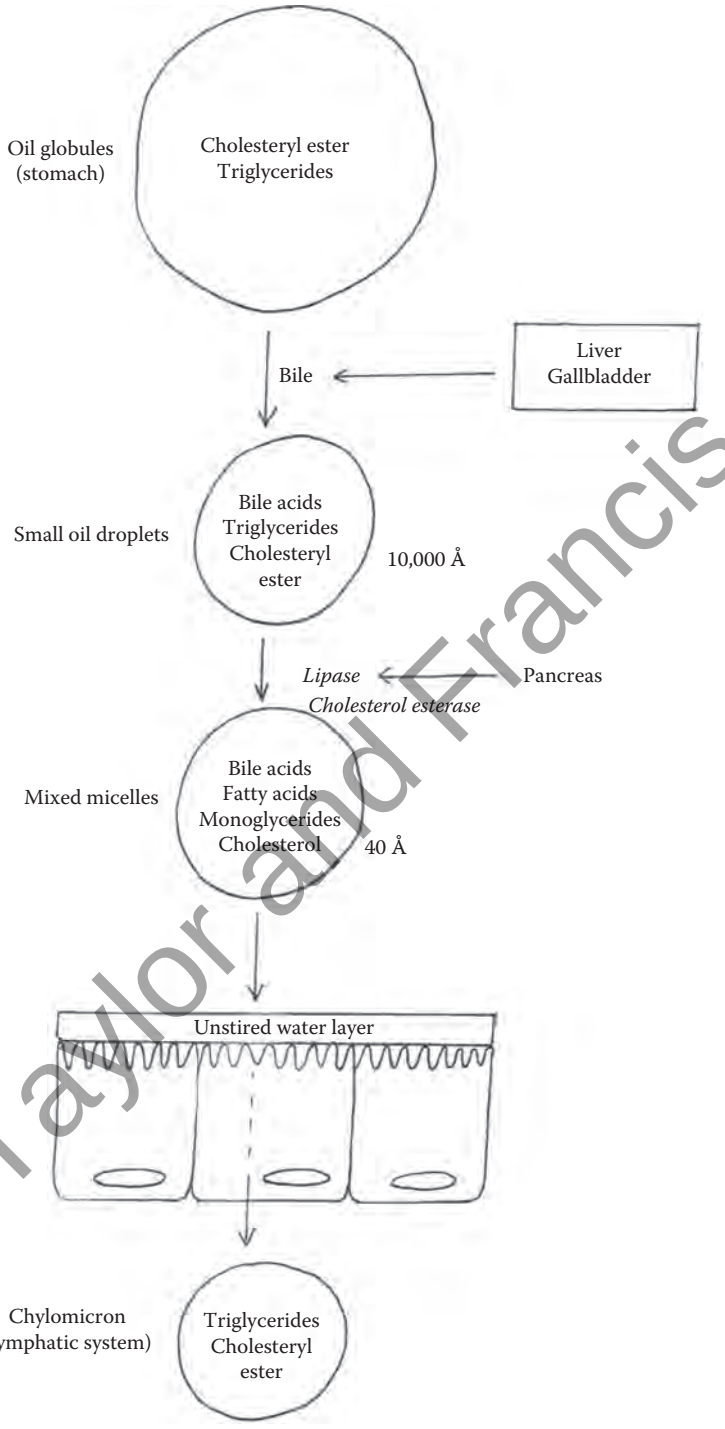



**FIGURE 1.53** 1-Deoxynojirimycin.

## APPENDIX

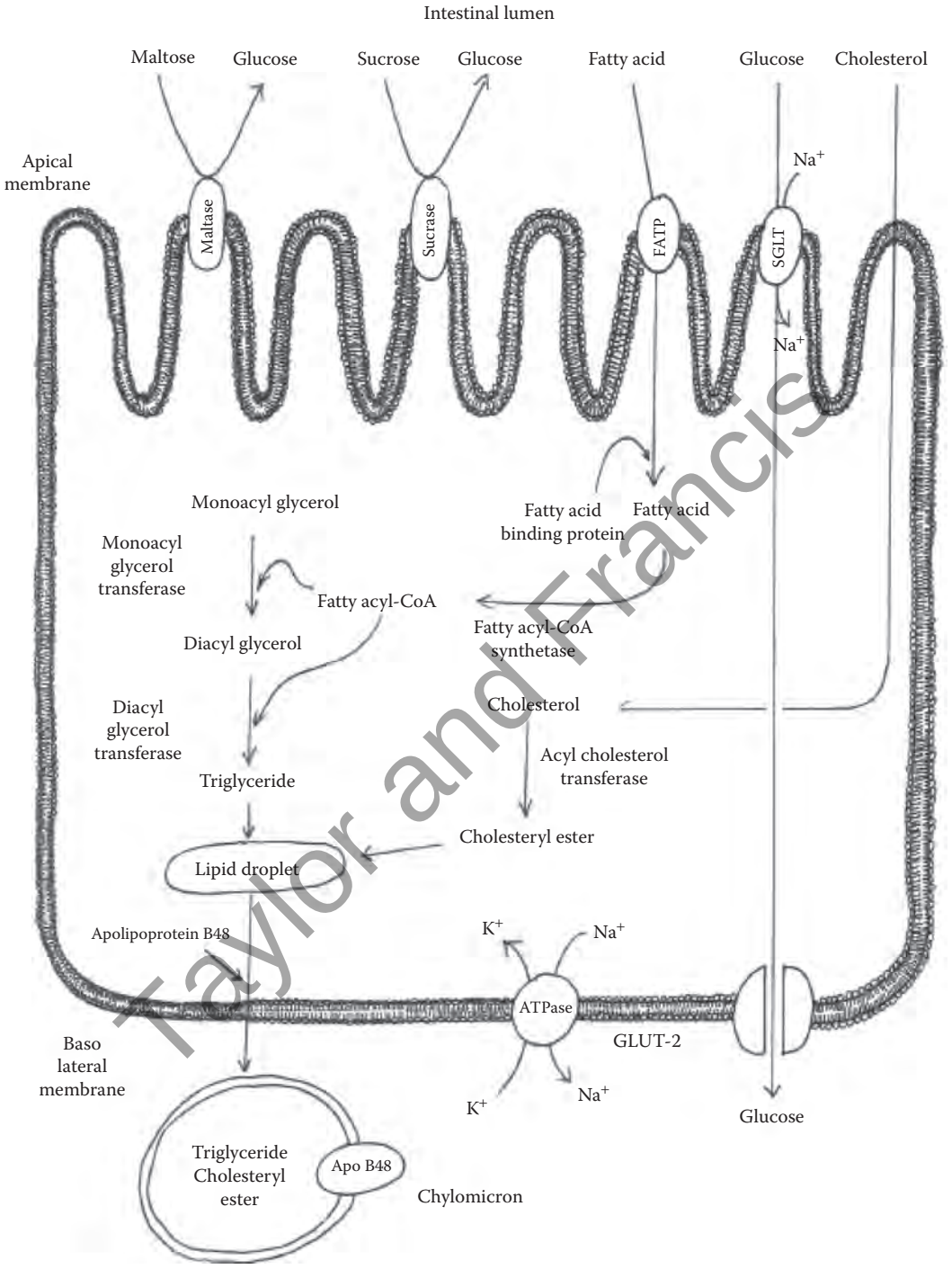



Appendix 1.1: Absorption of glucose, cholesterol and triglycerides.






Appendix 1.2: Emulsification of dietary fats.






Appendix 1.3: Absorption of glucose, fatty acids and cholesterol by enterocytes.

## REFERENCES


1. Ceriello, A., Cavarape, A., Martinelli, L., Da Ros, R., Marra, G., Quagliaro, L., Piconi, L., Assaloni, R. and Motz, E., 2004. The post-prandial state in type 2 diabetes and endothelial dysfunction: Effects of insulin aspart. *Diabetic Medicine*, 21(2), 171–175.
2. Delarue, J. and Magnan, C., 2007. Free fatty acids and insulin resistance. *Current Opinion in Clinical Nutrition & Metabolic Care*, 10(2), 142–148.
3. Fonseca, V., 2003. Clinical significance of targeting postprandial and fasting hyperglycemia in managing type 2 diabetes mellitus. *Current Medical Research and Opinion*, 19(7), 635–631.
4. Kahn, S.E., Hull, R.L. and Utzschneider, K.M., 2006. Mechanisms linking obesity to insulin resistance and type 2 diabetes. *Nature*, 444(7121), 840–846.
5. Liu, S. and Manson, J.E., 2001. Dietary carbohydrates, physical inactivity, obesity, and the 'metabolic syndrome'as predictors of corlonary heart disease. *Current Opinion in Lipidology*, 12(4), 395–404.
6. Shoelson, S.E., Herrero, L. and Naaz, A., 2007. Obesity, inflammation, and insulin resistance. *Gastroenterology*, 132(6), 2169–2180.
7. Hamosh, M., 1989. Lingual and gastric lipases. *Nutrition*, 6(6), 421–428.
8. Lee, Y.M., Kim, Y.S., Lee, Y., Kim, J., Sun, H., Kim, J.H. and Kim, J.S., 2012. Inhibitory activities of pancreatic lipase and phosphodiesterase from Korean medicinal plant extracts. *Phytotherapy Research*, 26(5), 778–782.
9. Yun, Y.R., Kim, M.J., Kwon, M.J., Kim, H.J., Song, Y.B., Song, K.B. and Song, Y.O., 2007. Lipid-lowering effect of hot water-soluble extracts of *Saururus chinensis* bail on rats fed high-fat diets. *Journal of Medicinal Food*, 10(2), 316–322.
10. Lin, A.H.M., Lee, B.H., Nichols, B.L., Quezada-Calvillo, R., Rose, D.R., Naim, H.Y. and Hamaker, B.R., 2012. Starch source influences dietary glucose generation at the mucosal α-glucosidase level. *Journal of Biological Chemistry*, 287(44), 36917–36921.
11. Krishna, M.S., Joy, B. and Sundaresan, A., 2015. Effect on oxidative stress, glucose uptake level and lipid droplet content by Apigenin 7, 4'-dimethyl ether isolated from *Piper longum* L. *Journal of Food Science and Technology*, 52(6), 3561–3570.
12. Robyt, J. and French, D., 1963. Action pattern and specificity of an amylase from *Bacillus subtilis*. *Archives of Biochemistry and Biophysics*, 100(3), 451–467.
13. Ono, Y., Hattori, E., Fukaya, Y., Imai, S. and Ohizumi, Y., 2006. Anti-obesity effect of *Nelumbo nucifera* leaves extract in mice and rats. *Journal of Ethnopharmacology*, 106(2), 238–244.
14. Ohkoshi, E., Miyazaki, H., Shindo, K., Watanabe, H., Yoshida, A., Yajima, H., 2007. Constituents from the leaves of *Nelumbo nucifera* stimulate lipolysis in the white adipose tissue of mice. *Planta Medica*, 73(12):1255–1259.
15. Lo Piparo, E., Scheib, H., Frei, N., Williamson, G., Grigorov, M. and Chou, C.J., 2008. Flavonoids for controlling starch digestion: Structural requirements for inhibiting human α-amylase. *Journal of Medicinal Chemistry*, 51(12), 3555–3561.
16. Liu, S., Li, D., Huang, B., Chen, Y., Lu, X. and Wang, Y., 2013. Inhibition of pancreatic lipase, α-glucosidase, α-amylase, and hypolipidemic effects of the total flavonoids from *Nelumbo nucifera* leaves. *Journal of Ethnopharmacology*, 149(1), 263–269.
17. Zhu, Y.T., Jia, Y.W., Liu, Y.M., Liang, J., Ding, L.S. and Liao, X., 2014. Lipase ligands in *Nelumbo nucifera* leaves and study of their binding mechanism. *Journal of Agricultural and Food Chemistry*, 62(44), 10679–10686.
18. Ahn, J.H., Kim, E.S., Lee, C., Kim, S., Cho, S.H., Hwang, B.Y. and Lee, M.K., 2013. Chemical constituents from *Nelumbo nucifera* leaves and their anti-obesity effects. *Bioorganic & Medicinal Chemistry Letters*, 23(12), 3604–3608.
19. Tuomilehto, J., Lindström, J., Eriksson, J.G., Valle, T.T., Hämäläinen, H., Ilanne-Parikka, P., Keinänen-Kiukaanniemi, S., Laakso, M., Louheranta, A., Rastas, M. and Salminen, V., 2001. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine*, 344(18), 1343–1350.
20. Liu, L., Yu, Y.L., Yang, J.S., Li, Y., Liu, Y.W., Liang, Y., Liu, X.D., Xie, L. and Wang, G.J., 2010. Berberine suppresses intestinal disaccharidases with beneficial metabolic effects in diabetic states, evidences from in vivo and in vitro study. *Naunyn-Schmiedeberg's Archives of Pharmacology*, 381(4), 371–381.
21. Yin, J., Xing, H. and Ye, J., 2008. Efficacy of berberine in patients with type 2 diabetes mellitus. *Metabolism*, 57(5), 712–717.
22. Lieberman, M., Marks, A.D. and Peet, A., 2013. *Marks' Basic Medical Biochemistry*. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins.

23. Patel, M.B. and Mishra, S.M., 2012. Magnoflorine from *Tinospora cordifolia* stem inhibits α-glucosidase and is antiglycemic in rats. *Journal of Functional Foods*, 4(1), 79–86.
24. Guang, J., Yi, D., Ming, Y. and Duan, Z., 1964. Pharmacological studies on magnoflorine, a hypotensive principle from Tu Qing Mu Xiang. *Acta Pharmaceutica Sinica*, 1, 5.
25. Rhoades, R.A. and Bell, D.R. (Eds.), 2012. *Medical Phisiology: Principles for Clinical Medicine*. Philadelphia, PA: Lippincott Williams & Wilkins.
26. Meddah, B., Ducroc, R., Faouzi, M.E.A., Eto, B., Mahraoui, L., Benhaddou-Andaloussi, A., Martineau, L.C., Cherrah, Y. and Haddad, P.S., 2009. Nigella sativa inhibits intestinal glucose absorption and improves glucose tolerance in rats. *Journal of Ethnopharmacology*, 121(3), 419–424.
27. Buchholz, T. and Melzig, M.F., 2016. Medicinal plants traditionally used for treatment of obesity and diabetes mellitus—screening for pancreatic lipase and α-amylase inhibition. *Phytotherapy Research*, 30(2), 260–266.
28. Wu, Q., Wang, Y. and Guo, M., 2011. Triterpenoid saponins from the seeds of celosia argentea and their anti-inflammatory and antitumor activities. *Chemical and Pharmaceutical Bulletin*, 59(5), 666–671.
29. Telagari, M. and Hullatti, K., 2015. In-vitro α-amylase and α-glucosidase inhibitory activity of *Adiantum caudatum Linn*. and *Celosia argentea Linn*. extracts and fractions. *Indian Journal of Pharmacology*, 47(4), p. 425.
30. Bauer, E., Jakob, S. and Mosenthin, R., 2005. Principles of physiology of lipid digestion. *Asian-Australasian Journal of Animal Sciences*, 18(2), 282–295.
31. Vinarova, L., Vinarov, Z., Atanasov, V., Pantcheva, I., Tcholakova, S., Denkov, N. and Stoyanov, S., 2015. Lowering of cholesterol bioaccessibility and serum concentrations by saponins: In vitro and in vivo studies. *Food & Function*, 6(2), 501–512.
32. Han, L.K., Nose, R., Li, W., Gong, X.J., Zheng, Y.N., Yoshikawa, M., Koike, K., Nikaido, T., Okuda, H. and Kimura, Y., 2006. Reduction of fat storage in mice fed a high-fat diet long term by treatment with saponins prepared from *Kochia scoparia* fruit. *Phytotherapy Research*, 20(10), 877–882.
33. Kasabri, V., Afifi, F.U. and Hamdan, I., 2011. In vitro and in vivo acute antihyperglycemic effects of five selected indigenous plants from Jordan used in traditional medicine. *Journal of Ethnopharmacology*, 133(2), 888–896.
34. Goel, V., Ooraikul, B. and Basu, TK., 1997. Cholesterol lowering effects of rhubarb stalk fiber in hypercholesterolemic men. *The American College of Nutrition*, 16(6), 600–604.
35. Thielecke, F. and Boschmann, M., 2009. The potential role of green tea catechins in the prevention of the metabolic syndrome–a review. *Phytochemistry*, 70(1), 11–24.
36. Surwit, R.S., Kuhn, C.M., Cochrane, C., McCubbin, J.A. and Feinglos, M.N., 1988. Diet-induced type II diabetes in C57BL/6J mice. *Diabetes*, 37(9), 1163–1167.
37. Grove, K.A., Sae-Tan, S., Kennett, M.J. and Lambert, J.D., 2012. (−)− Epigallocatechin-3-gallate inhibits pancreatic lipase and reduces body weight gain in high fat-fed obese mice. *Obesity*, 20(11), 2311–2313.
38. Fei, Q., Gao, Y., Zhang, X., Sun, Y., Hu, B., Zhou, L., Jabbar, S. and Zeng, X., 2014. Effects of oolong tea polyphenols, EGCG, and EGCG3 Me on pancreatic α-amylase activity in vitro. *Journal of Agricultural and Food Chemistry*, 62(39), 9507–9514.
39. Ryu, H.W., Cho, J.K., Curtis-Long, M.J., Yuk, H.J., Kim, Y.S., Jung, S., Kim, Y.S., Lee, B.W. and Park, K.H., 2011. α-Glucosidase inhibition and antihyperglycemic activity of prenylated xanthones from *Garcinia mangostana*. *Phytochemistry*, 72(17), 2148–2154.
40. Gowri, P.M., Tiwari, A.K., Ali, A.Z. and Rao, J.M., 2007. Inhibition of α-glucosidase and amylase by bartogenic acid isolated from *Barringtonia racemosa* Roxb. seeds. *Phytotherapy Research*, 21(8), 796–799.
41. Ponnapalli, M.G., Sukki, S., Annam, S.C.V.A.R., Ankireddy, M., Tirunagari, H., Tuniki, V.R. and Bobbili, V.P., 2015. α-Glucosidase inhibitory monoacylated polyhydroxytriterpenoids from the fruits of *Barringtonia racemosa*. *Tetrahedron Letters*, 56(12), 1570–1574.
42. Mbaze, L.M.A., Poumale, H.M.P., Wansi, J.D., Lado, J.A., Khan, S.N., Iqbal, M.C., Ngadjui, B.T. and Laatsch, H., 2007. α-Glucosidase inhibitory pentacyclic triterpenes from the stem bark of *Fagara tessmannii* (Rutaceae). *Phytochemistry*, 68(5), 591–595.
43. Dang, P.H., Nguyen, N.T., Nguyen, H.X., Nguyen, L.B., Le, T.H., Van Do, T.N., Van Can, M. and Nguyen, M.T.T., 2015. α-Glucosidase inhibitors from the leaves of *Embelia ribes*. *Fitoterapia*, 100, 201–207.
44. Dang, P.H., Nguyen, H.X., Nguyen, N.T., Le, H.N.T. and Nguyen, M.T.T., 2014. α-Glucosidase inhibitors from the stems of *Embelia ribes*. *Phytotherapy Research*, 28(11), 1632–1636.
45. Weibel, E.K., Hadvary, P., Hochuli, E., Kupfer, E. and Lengsfeld, H., 1987. Lipstatin, an inhibitor of pancreatic lipase, produced by *Streptomyces toxytricini*. *The Journal of Antibiotics*, 40(8), 1081–1085.

46. Ballinger, A. and Peikin, S.R., 2002. Orlistat: Its current status as an anti-obesity drug. *European Journal of Pharmacology*, 440(2), 109–117.
47. Megalli, S., Davies, N.M. and Roufogalis, B.D., 2006. Anti-hyperlipidemic and hypoglycemic effects of *Gynostemma pentaphyllum* in the zucker fatty rat. *Journal of Pharmacy and Pharmaceutical Sciences*, 9(3), 281–291.
48. Yang, Y.H., Yang, J. and Jiang, Q.H., 2013. Hypolipidemic effect of gypenosides in experimentally induced hypercholesterolemic rats. *Lipids in Health and Disease*, 12(1), 154.
49. Kwiterovich, P.O., 2012. *The John Hopkins Textbook of Dyslipidemia*. Philadelphia, PA: Lippincott Williams & Wilkins.
50. Su, J., Wang, H., Ma, C., Liu, C., Rahman, M.T., Gao, C. and Nie, R., 2016. Hypolipidemic mechanism of gypenosides via inhibition of pancreatic lipase and reduction in cholesterol micellar solubility. *European Food Research and Technology*, 242(3), 305–312.
51. Hau, J. and Schapiro, S.J. (Eds.), 2010. *Handbook of Laboratory Animal Science*, *Volume I: Essential Principles and Practices*. Boca Raton, FL: CRC Press.
52. Ikeda, I. and Sugano, M., 1998. Inhibition of cholesterol absorption by plant sterols for mass intervention. *Current Opinion in Lipidology*, 9(6), 527–531.
53. Plat, J. and Mensink, R.P., 2001. Effects of plant sterols and stanols on lipid metabolism and cardiovascular risk. *Nutrition, Metabolism, and Cardiovascular Diseases: NMCD*, 11(1), 31–40.
54. Kalsait, R.P., Khedekar, P.B., Saoji, A.N. and Bhusari, K.P., 2011. Isolation of phytosterols and antihyperlipidemic activity of *Lagenaria siceraria*. *Archives of Pharmacal Research*, 34(10), 1599–1604.
55. Chiasson, J.L., Josse, R.G., Gomis, R., Hanefeld, M., Karasik, A., Laakso, M. and STOP-NIDDM Trial Research Group, 2002. Acarbose for prevention of type 2 diabetes mellitus: The STOP-NIDDM randomised trial. *The Lancet*, 359(9323), 2072–2077.
56. Suzuki, Y.A., Murata, Y., Inui, H., Sugiura, M. and Nakano, Y., 2005. Triterpene glycosides of *Siraitia grosvenori* inhibit rat intestinal maltase and suppress the rise in blood glucose level after a single oral administration of maltose in rats. *Journal of Agricultural and Food Chemistry*, 53(8), 2941–2946.
57. Ali, L., Khan, A.K.A., Mamun, M.I.R., Mosihuzzaman, M., Nahar, N., Nur-e-Alam, M. and Rokeya, B., 1993. Studies on hypoglycemic effects of fruit pulp, seed, and whole plant of *Momordica charantia* on normal and diabetic model rats. *Planta Medica*, 59(05), 408–412.
58. Sankhari, J.M., Thounaojam, M.C., Jadeja, R.N., Devkar, R.V. and Ramachandran, A.V., 2012. Anthocyanin-rich red cabbage (*Brassica oleracea* L.) extract attenuates cardiac and hepatic oxidative stress in rats fed an atherogenic diet. *Journal of the Science of Food and Agriculture*, 92(8), 1688–1693.
59. Dyer, J., Wood, I.S., Palejwala, A., Ellis, A. and Shirazi-Beechey, S.P., 2002. Expression of monosaccharide transporters in intestine of diabetic humans. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, 282(2), G241–G248.
60. Matsuda, H., Asao, Y., Nakamura, S., Hamao, M., Sugimoto, S., Hongo, M., Pongpiriyadacha, Y. and Yoshikawa, M., 2009. Antidiabetogenic constituents from the Thai traditional medicine *Cotylelobium melanoxylon*. *Chemical and Pharmaceutical Bulletin*, 57(5), 487–494.
61. Morikawa, T., Chaipech, S., Matsuda, H., Hamao, M., Umeda, Y., Sato, H., Tamura, H., Ninomiya, K., Yoshikawa, M., Pongpiriyadacha, Y. and Hayakawa, T., 2012. Anti-hyperlipidemic constituents from the bark of *Shorea roxburghii*. *Journal of Natural Medicines*, 66(3), 516–524.
62. Morikawa, T., Chaipech, S., Matsuda, H., Hamao, M., Umeda, Y., Sato, H., Tamura, H., Kon'i, H., Ninomiya, K., Yoshikawa, M. and Pongpiriyadacha, Y., 2012. Antidiabetogenic oligostilbenoids and 3-ethyl-4-phenyl-3, 4-dihydroisocoumarins from the bark of *Shorea roxburghii*. *Bioorganic & Medicinal Chemistry*, 20(2), 832–840.
63. Ahn, J.H., Liu, Q., Lee, C., Ahn, M.J., Yoo, H.S., Hwang, B.Y. and Lee, M.K., 2012. A new pancreatic lipase inhibitor from *Broussonetia kanzinoki*. *Bioorganic & Medicinal Chemistry Letters*, 22(8), 2760–2763.
64. Shrayyef, M.Z. and Gerich, J.E., 2010. Normal glucose homeostasis. In *Principles of Diabetes Mellitus*, Poretsky, L., (Ed.). New York: Springer, pp. 19–35.
65. Leu, J.P. and Zonszein, J., 2010. Diagnostic criteria and classification of diabetes. In *Principles of Diabetes Mellitus,* Poretsky, L., (Ed.). New York: Springer, pp. 107–115.
66. Herzlinger, S. and Martin, J.A., 2010. Treating type 2 diabetes mellitus. In *Principles of Diabetes Mellitus*, Poretsky, L., (Ed.). New York: Springer, pp. 731–747..
67. Choo, C.Y., Sulong, N.Y., Man, F. and Wong, T.W., 2012. Vitexin and isovitexin from the leaves of *Ficus deltoidea* with in-vivo α-glucosidase inhibition. *Journal of Ethnopharmacology*, 142(3), 776–781.
68. Yang, J.P., He, H. and Lu, Y.H., 2014. Four flavonoid compounds from *Phyllostachys edulis* leaf extract retard the digestion of starch and its working mechanisms. *Journal of Agricultural and Food Chemistry*, 62(31), 7760–7770.

69. Kumar, S., Kumar, D., Deshmukh, R.R., Lokhande, P.D., More, S.N. and Rangari, V.D., 2008. Antidiabetic potential of *Phyllanthus reticulatus* in alloxan-induced diabetic mice. *Fitoterapia*, 79(1), 21–23.
70. Pojchaijongdee, N., Sotanaphun, U., Limsirichaikul, S. and Poobrasert, O., 2010. Geraniinic acid derivative from the leaves of *Phyllanthus reticulatus*. *Pharmaceutical Biology*, 48(7), 740–744.
71. Espín, J.C., González-Barrio, R., Cerdá, B., López-Bote, C., Rey, A.I. and Tomás-Barberán, F.A., 2007. Iberian pig as a model to clarify obscure points in the bioavailability and metabolism of ellagitannins in humans. *Journal of Agricultural and Food Chemistry*, 55(25), 10476–10485.
72. Maruthappan, V. and Shree, K.S., 2010. Effects of Phyllanthus reticulatus on lipid profile and oxidative stress in hypercholesterolemic albino rats. *Indian Journal of Pharmacology*, 42(6), 388.
73. Rahmatullah, M., Hasan, S.K., Ali, Z., Rahman, S. and Jahan, R., 2012. Antihyperglycemic and antinociceptive activities of methanolic extract of *Euphorbia thymifolia* L. whole plants. *Journal of Chinese Integrative Medicine*, 10(2): 228–232.
74. Amaral, A.C.F., Kuster, R.M., Gonçalves, J.L.S. and Wigg, M.D., 1999. Antiviral investigation on the flavonoids of *Chamaesyce thymifolia*. *Fitoterapia*, 70(3), 293–295.
75. Lee, S.H., Tanaka, T., Nonaka, G.I. and Nishioka, I., 1990. Hydrolysable tannins from *Euphorbia thymifolia*. *Phytochemistry*, 29(11), 3621–3625.
76. Yoshikawa, M., Wang, T., Morikawa, T., Xie, H. and Matsuda, H., 2007. Bioactive constituents from Chinese natural medicines. XXIV. Hypoglycemic effects of *Sinocrassula indica* in sugar-loaded rats and genetically diabetic KK-Ay mice and structures of new acylated flavonol glycosides, sinocrassosides A1, A2, B1, and B2. *Chemical and Pharmaceutical Bulletin*, 55(9), 1308–1315.
77. Wright, E.M., Martín, M.G. and Turk, E., 2003. Intestinal absorption in health and disease—sugars. *Best Practice & Research Clinical Gastroenterology*, 17(6), 943–956.
78. Hediger, M.A., Turk, E. and Wright, E.M., 1989. Homology of the human intestinal Na+/glucose and *Escherichia coli* Na+/proline cotransporters. *Proceedings of the National Academy of Sciences*, 86(15), 5748–5752.
79. Wright, E.M., Martín, M.G. and Turk, E., 2003. Intestinal absorption in health and disease—sugars. *Best Practice & Research Clinical Gastroenterology*, 17(6), 943–956.
80. Islam, M.N., Jung, H.A., Sohn, H.S., Kim, H.M. and Choi, J.S., 2013. Potent α-glucosidase and protein tyrosine phosphatase 1B inhibitors from *Artemisia capillaris*. *Archives of Pharmacal Research*, 36(5), 542–552.
81. Sabu, M.C. and Kuttan, R., 2009. Antidiabetic and antioxidant activity of *Terminalia belerica*. Roxb. *Indian Journal of Experimental Biology*, 47, 270–275.
82. Makihara, H., Shimada, T., Machida, E., Oota, M., Nagamine, R., Tsubata, M., Kinoshita, K., Takahashi, K. and Aburada, M., 2012. Preventive effect of *Terminalia bellirica* on obesity and metabolic disorders in spontaneously obese type 2 diabetic model mice. *Journal of Natural Medicines*, 66(3), 459–467.
83. Wansi, J.D., Lallemand, M.C., Chiozem, D.D., Toze, F.A.A., Mbaze, L.M.A., Naharkhan, S., Iqbal, M.C., Tillequin, F., Wandji, J. and Fomum, Z.T., 2007. α-Glucosidase inhibitory constituents from stem bark of *Terminalia superba* (Combretaceae). *Phytochemistry*, 68(15), 2096–2100.
84. Bruneton, J., 1987. *Elements de phytochimie et de pharmacognosy*. Paris, France: Lavoisier.
85. Madhavi, D.L., Bomser, J., Smith, M.A.L. and Singletary, K., 1998. Isolation of bioactive constituents from *Vaccinium myrtillus* (bilberry) fruits and cell cultures. *Plant Science*, 131(1), 95–103.
86. Tadera, K., Minami, Y., Takamatsu, K. and Matsuoka, T., 2006. Inhibition of α-glucosidase and α-amylase by flavonoids. *Journal of Nutritional Science and Vitaminology*, 52(2), 149–153.
87. Rudel, L.L., Lee, R.G. and Cockman, T.L., 2001. Acyl coenzyme A: Cholesterol acyltransferase types 1 and 2: Structure and function in atherosclerosis. *Current Opinion in Lipidology*, 12(2), 121–127.
88. Liang, Y., Chen, J., Zuo, Y., Ma, K.Y., Jiang, Y., Huang, Y. and Chen, Z.Y., 2013. Blueberry anthocyanins at doses of 0.5 and 1% lowered plasma cholesterol by increasing fecal excretion of acidic and neutral sterols in hamsters fed a cholesterol-enriched diet. *European Journal of Nutrition*, 52(3), 869–875.
89. Martínez, I., Wallace, G., Zhang, C., Legge, R., Benson, A.K., Carr, T.P., Moriyama, E.N. and Walter, J., 2009. Diet-induced metabolic improvements in a hamster model of hypercholesterolemia are strongly linked to alterations of the gut microbiota. *Applied and Environmental Microbiology*, 75(12), 4175–4184.
90. Ichiyanagi, T., Shida, Y., Rahman, M.M., Hatano, Y. and Konishi, T., 2006. Bioavailability and tissue distribution of anthocyanins in bilberry (*Vaccinium myrtillus* L.) extract in rats. *Journal of Agricultural and Food Chemistry*, 54(18), 6578–6587.
91. Güder, A., Gür, M. and Engin, M.S., 2015. Antidiabetic and antioxidant properties of bilberry (*Vaccinium myrtillus Linn.*) fruit and their chemical composition. *Journal of Agricultural Science and Technology*, 17(2), 387–400.

92. Garcia, F., 1941. Distribution and deterioration of insulin-like principle in *Lagerstroemia speciosa* (banaba). *Acta Med Philippina*, 3, 99–104.
93. Saumya, S.M. and Basha, P.M., 2011. Antioxidant effect of *Lagerstroemia speciosa Pers* (Banaba) leaf extract in streptozotocin-induced diabetic mice. *Indian Journal of Experimental Biology*, 49(2), 125–131.
94. Takagi, S., Miura, T., Ishihara, E., Ishida, T., and Chinzei, Y., 2010. Effect of corosolic acid on dietary hypercholesterolemia and hepatic steatosis in KK-Ay diabetic mice. *Biomedical Research*, 31(4): 213–218.
95. Hou, W., Li, Y., Zhang, Q., Wei, X., Peng, A., Chen, L. and Wei, Y., 2009. Triterpene acids isolated from *Lagerstroemia speciosa* leaves as α-glucosidase inhibitors. *Phytotherapy Research*, 23(5), 614–618.
96. Buchholz, T. and Melzig, M.F., 2016. Medicinal plants traditionally used for treatment of obesity and diabetes mellitus–screening for pancreatic lipase and α-amylase inhibition. *Phytotherapy Research*, 30(2), 260–266.
97. Bellesia, A., Verzelloni, E. and Tagliazucchi, D., 2015. Pomegranate ellagitannins inhibit α-glucosidase activity in vitro and reduce starch digestibility under simulated gastro-intestinal conditions. *International Journal of Food Sciences and Nutrition*, 66(1), 85–92.
98. Kawakami, K., Li, P., Uraji, M., Hatanaka, T. and Ito, H., 2014. Inhibitory effects of pomegranate extracts on recombinant human maltase–glucoamylase. *Journal of Food Science*, 79(9), H1848–H1853.
99. Yasuda, M., Yasutake, K., Hino, M., Ohwatari, H., Ohmagari, N., Takedomi, K., Tanaka, T. and Nonaka, G.I., 2014. Inhibitory effects of polyphenols from water chestnut (Trapa japonica) husk on glycolytic enzymes and postprandial blood glucose elevation in mice. *Food Chemistry*, 165, 42–49.
100. Gupta, S., Sharma, S.B., Prabhu, K.M. and Bansal, S.K., 2009. Protective role of *Cassia auriculata* leaf extract on hyperglycemia-induced oxidative stress and its safety evaluation. *Indian Journal of Biochemistry & Biophysics,* 46(5), 371–377.
101. Habtemariam, S., 2013. Antihyperlipidemic components of *Cassia auriculata* aerial parts: Identification through in vitro studies. *Phytotherapy Research*, 27(1), 152–155.
102. Dendup, T., Prachyawarakorn, V., Pansanit, A., Mahidol, C., Ruchirawat, S. and Kittakoop, P., 2014. α-Glucosidase inhibitory activities of isoflavanones, isoflavones, and pterocarpans from *Mucuna pruriens*. *Planta Medica*, 80(7), 604–608.
103. Abesundara, K.J., Matsui, T. and Matsumoto, K., 2004. α-Glucosidase inhibitory activity of some Sri Lanka plant extracts, one of which, *Cassia auriculata*, exerts a strong antihyperglycemic effect in rats comparable to the therapeutic drug acarbose. *Journal of Agricultural and Food Chemistry*, 52(9), 2541–2545.
104. Maurya, R., Ray, A.B., Duah, F.K., Slatkin, D.J. and Schiff Jr, P.L., 1984. Constituents of *Pterocarpus marsupium*. *Journal of Natural Products*, 47(1), 179–181.
105. Bai, Y.P., Zhang, G.G., Shi, R.Z., Li, Y.J., Tan, G.S. and Chen, J., 2006. Inhibitory effect of reinioside C on LOX-1 expression induced by OX-LDL. *Journal of Central South University Medical Sciences*, 31(5), 659–662.
106. Ros, E., 2000. Intestinal absorption of triglyceride and cholesterol. Dietary and pharmacological inhibition to reduce cardiovascular risk. *Atherosclerosis*, 151(2), 357–379.
107. Li, H., Wang, Q.J., Zhu, D.N. and Yang, Y., 2008. Reinioside C, a triterpene saponin of *Polygala aureocauda* Dunn, exerts hypolipidemic effect on hyperlipidemic mice. *Phytotherapy Research*, 22(2), 159–164.
108. Kawaguchi, K., Mizuno, T., Aida, K. and Uchino, K., 1997. Hesperidin as an inhibitor of lipases from porcine pancreas and Pseudomonas. *Bioscience, Biotechnology, and Biochemistry*, 61(1), 102–104.
109. Uvarani, C., Sankaran, M., Jaivel, N., Chandraprakash, K., Ata, A. and Mohan, P.S., 2013. Bioactive dimeric carbazole alkaloids from *Murraya koenigii*. *Journal of Natural Products*, 76(6), 993–1000.
110. Birari, R., Javia, V. and Bhutani, K.K., 2010. Antiobesity and lipid lowering effects of *Murraya koenigii* (L.) Spreng leaves extracts and mahanimbine on high-fat diet induced obese rats. *Fitoterapia*, 81(8), 1129–1133.
111. Birari, R., Roy, S.K., Singh, A. and Bhutani, K.K., 2009. Pancreatic lipase inhibitory alkaloids of *Murraya koenigii* leaves. *Natural Product Communications*, 4(8), 1089–1092.
112. Park, Y.D., Lee, W.S., An, S. and Jeong, T.S., 2007. Human acyl-CoA: Cholesterol acyltransferase inhibitory activities of aliphatic acid amides from *Zanthoxylum piperitum* DC. *Biological and Pharmaceutical Bulletin*, 30(1), 205–207.
113. Giordani, M.A., Collicchio, T.C.M., Ascêncio, S.D., de Oliveira Martins, D.T., Balogun, S.O., Bieski, I.G.C., da Silva, L.A., Colodel, E.M., de Souza, R.L., de Souza, D.L.P. and de França, S.A., 2015. Hydroethanolic extract of the inner stem bark of *Cedrela odorata* has low toxicity and reduces hyperglycemia induced by an overload of sucrose and glucose. *Journal of Ethnopharmacology*, 162, 352–361.

114. Prashanth, D., Amit, A., Samiulla, D.S., Asha, M.K. and Padmaja, R., 2001. α-Glucosidase inhibitory activity of *Mangifera indica* bark. *Fitoterapia*, 72(6), 686–688.
115. Uddin, G., Rauf, A., Al-Othman, A.M., Collina, S., Arfan, M., Ali, G. and Khan, I., 2012. Pistagremic acid, a glucosidase inhibitor from *Pistacia integerrima*. *Fitoterapia*, 83(8), 1648–1652.
116. Kasabri, V., Afifi, F.U. and Hamdan, I., 2011. In vitro and in vivo acute antihyperglycemic effects of five selected indigenous plants from Jordan used in traditional medicine. *Journal of Ethnopharmacology*, 133(2), 888–896.
117. Williams, J.A., Choe, Y.S., Noss, M.J., Baumgartner, C.J. and Mustad, V.A., 2007. Extract of Salacia oblonga lowers acute glycemia in patients with type 2 diabetes. *The American Journal of Clinical Nutrition*, 86(1), 124–130.
118. Li, Y., Peng, G., Li, Q., Wen, S., Huang, T.H.W., Roufogalis, B.D. and Yamahara, J., 2004. *Salacia oblonga* improves cardiac fibrosis and inhibits postprandial hyperglycemia in obese zucker rats. *Life Sciences*, 75(14), 1735–1746.
119. Matsuda, H., Murakami, T., Yashiro, K., Yamahara, J. and Yoshikawa, M., 1999. Antidiabetic principles of natural medicines. IV. Aldose reductase and α-glucosidase inhibitors from the roots of *Salacia oblonga* wall. (Celastraceae): Structure of a new friedelane-type triterpene, kotalagenin 16-acetate. *Chemical and Pharmaceutical Bulletin*, 47(12), 1725–1729.
120. Karunanayake, E.H., Welihinda, J., Sirimanne, S.R. and Adorai, G.S., 1984. Oral hypoglycaemic activity of some medicinal plants of Sri Lanka. *Journal of Ethnopharmacology*, 11(2), 223–231.
121. Yoshikawa, M., Shimoda, H., Nishida, N., Takada, M. and Matsuda, H., 2002. *Salacia reticulata* and its polyphenolic constituents with lipase inhibitory and lipolytic activities have mild antiobesity effects in rats. *The Journal of Nutrition*, 132(7), 1819–1824.
122. Yoshino, K., Miyauchi, Y., Kanetaka, T., Takagi, Y. and Koga, K., 2009. Anti-diabetic activity of a leaf extract prepared from *Salacia reticulata* in mice. *Bioscience, Biotechnology, and Biochemistry*, 73(5), 1096–1104.
123. Avcı, G., Kupeli, E., Eryavuz, A., Yesilada, E. and Kucukkurt, I., 2006. Antihypercholesterolaemic and antioxidant activity assessment of some plants used as remedy in Turkish folk medicine. *Journal of Ethnopharmacology*, 107(3), 418–423.
124. Fukunaga, T., Kajikawa, I., Nishiya, K., Watanabe, Y., Takeya, K. and Itokawa, H., 1987. Studies on the constituents of the European mistletoe, *Viscum album* L. *Chemical and Pharmaceutical Bulletin*, 35(8), 3292–3297.
125. Wollenweber, E., Wieland, A. and Haas, K., 2000. Epicuticular waxes and flavonol aglycones of the European mistletoe, *Viscum album* L. *Zeitschrift Für Naturforschung C*, 55(5–6), 314–317.
126. Iwai, K., Onodera, A. and Matsue, H., 2004. Inhibitory effects of *Viburnum dilatatum* Thunb.(gamazumi) on oxidation and hyperglycemia in rats with streptozotocin-induced diabetes. *Journal of Agricultural and Food Chemistry*, 52(4), 1002–1007.
127. Iwai, K., Kim, M.Y., Onodera, A. and Matsue, H., 2006. α-Glucosidase Inhibitory and antihyperglycemic effects of polyphenols in the fruit of *Viburnum dilatatum* Thunb. *Journal of Agricultural and Food Chemistry*, 54(13), 4588–4592.
128. Wu, T., Yu, Z., Tang, Q., Song, H., Gao, Z., Chen, W. and Zheng, X., 2013. Honeysuckle anthocyanin supplementation prevents diet-induced obesity in C57BL/6 mice. *Food & Function*, 4(11), 1654–1661.
129. Gau, S.W., Chen, C.C., Chen, Y.P. and Hsu, H.Y., 1983. Constituents of Ilex species I. On the leaves of *Ilex cornuta* Lindl. *Journal of the Chinese Chemical Society*, 30(3), 185–188.
130. Im, K.R., Jeong, T.S., Kwon, B.M., Baek, N.I., Kim, S.H. and Kim, D.K., 2006. Acyl-CoA: Cholesterol acyltransferase inhibitors from *Ilex macropoda*. *Archives of Pharmacal Research*, 29(3), 191–194.
131. Baek, M.Y., Cho, J.G., Lee, D.Y., Ann, E.M., Jeong, T.S. and Baek, N.I., 2010. Isolation of triterpenoids from the stem bark of *Albizia julibrissin* and their inhibition activity on ACAT-1 and ACAT-2. *Journal of the Korean Society for Applied Biological Chemistry*, 53(3), 310–315.
132. Wang, Z.B., Jiang, H., Xia, Y.G., Yang, B.Y. and Kuang, H.X., 2012. α-Glucosidase inhibitory constituents from *Acanthopanax senticosus* harm leaves. *Molecules*, 17(6), 6269–6276.
133. Li, F., Li, W., Fu, H., Zhang, Q. and Koike, K., 2007. Pancreatic lipase-inhibiting triterpenoid saponins from fruits of *Acanthopanax senticosus*. *Chemical and Pharmaceutical Bulletin*, 55(7), 1087–1089.
134. Li, J.L., Li, N., Lee, H.S., Xing, S.S., Qi, S.Z., Tuo, Z.D., Zhang, L., Wang, X.B. and Cui, L., 2016. Inhibition effect of neo-lignans from *Eleutherococcus senticosus* (Rupt. & maxim.) Maxim on diacylglycerol acyltransferase (DGAT). *Phytochemistry Letters*, 15, 147–151.
135. Durrington, P., 2007. *Hyperlipidaemia: Diagnosis and Management*, 3rd ed. Boca Raton, FL: CRC Press.

136. Chan, H.H., Sun, H.D., Reddy, M.V.B. and Wu, T.S., 2010. Potent α-glucosidase inhibitors from the roots of *Panax japonicus* CA Meyer var. major. *Phytochemistry*, 71(11), 1360–1364.
137. Supkamonseni, N., Thinkratok, A., Meksuriyen, D. and Srisawat, R., 2014. Hypolipidemic and hypoglycemic effects of *Centella asiatica* (L.) extract in vitro and in vivo. *Indian Journal of Experimental Biology*, 52(10), 965–971.
138. Mo, E.J., Yang, H.J., Jeong, J.Y., Kim, S.B., Liu, Q., Hwang, B.Y. and Lee, M.K., 2016. Pancreatic lipase inhibitory phthalide derivatives from the rhizome of *Cnidium officinale*. *Records of Natural Products*, 10(2), 148.
139. Brindis, F., Rodríguez, R., Bye, R., González-Andrade, M. and Mata, R., 2010. (Z)-3-Butylidenephthalide from *Ligusticum porteri*, an α-glucosidase inhibitor. *Journal of Natural Products*, 74(3), 314–320.
140. Shalaby, N.M., Abd-Alla, H.I., Aly, H.F., Albalawy, M.A., Shaker, K.H. and Bouajila, J., 2014. Preliminary in vitro and in vivo evaluation of antidiabetic activity of *Ducrosia anethifolia* Boiss. and its linear furanocoumarins. *BioMed Research International*, 2014, 13.
141. Gupta, R.K., Kesari, A.N., Murthy, P.S., Chandra, R., Tandon, V. and Watal, G., 2005. Hypoglycemic and antidiabetic effect of ethanolic extract of leaves of *Annona squamosa* L. in experimental animals. *Journal of Ethnopharmacology*, 99(1), 75–81.
142. Nukitrangsan, N., Okabe, T., Toda, T., Inafuku, M., Iwasaki, H. and Oku, H., 2012. Effect of *Peucedanum japonicum* Thunb extract on high-fat diet-induced obesity and gene expression in mice. *Journal of Oleo Science*, 61(2), 89–101.
143. Lee, J.S., Choi, M.S., Seo, K.I., Lee, J., Lee, H.I., Lee, J.H., Kim, M.J. and Lee, M.K., 2014. Platycodi radix saponin inhibits α-glucosidase in vitro and modulates hepatic glucose-regulating enzyme activities in C57BL/KsJ-db/db mice. *Archives of Pharmacal Research*, 37(6), 773–782.
144. Owen, J.B., Treasure, J.L. and Collier, D.A. (Eds.), 2001. *Animal Models-Disorders of Eating Behaviour and Body Composition*. Dordrecht, the Netherlands: Kluwer Academic Publishers.
145. Hamza, N., Berke, B., Cheze, C., Le Garrec, R., Lassalle, R., Agli, AN., Robinson, P., Gin, H. and Moore, N., 2011. Treatment of high-fat diet induced type 2 diabetes in C57BL/6J mice by two medicinal plants used in traditional treatment of diabetes in the east of Algeria. *Journal of Ethnopharmacology*, 133(2), 931–933.
146. Boudjelal, A., Siracusa, L., Henchiri, C., Sarri, M., Abderrahim, B., Baali, F. and Ruberto, G., 2015. Antidiabetic effects of aqueous infusions of artemisia herba-alba and ajuga iva in alloxan-induced diabetic rats. *Planta Medica*, 81(9), 696–704.
147. Takahashi, T. and Miyazawa, M., 2012. Potent α-glucosidase inhibitors from safflower (*Carthamus tinctorius* L.) seed. *Phytotherapy Research*, 26(5), 722–726.
148. Wafo, P., Kamdem, R.S., Ali, Z., Anjum, S., Begum, A., Oluyemisi, O.O., Khan, S.N., Ngadjui, B.T., Etoa, X.F. and Choudhary, M.I., 2011. Kaurane-type diterpenoids from *Chromoleana odorata*, their X-ray diffraction studies and potent α-glucosidase inhibition of 16-kauren-19-oic acid. *Fitoterapia*, 82(4), 642–646.
149. Zareen, S., Choudhary, M.I., Akhtar, M.N. and Khan, S.N., 2008. α-Glucosidase inhibitory activity of triterpenoids from *Cichorium intybus*. *Journal of Natural Products*, 71(5), 910–913.
150. Trautwein, E.A., Rieckhoff, D. and Erbersdobler, H.F., 1998. Dietary inulin lowers plasma cholesterol and triacylglycerol and alters biliary bile acid profile in hamsters. *The Journal of Nutrition*, 128(11), 1937–1943.
151. Roberfroid, M.B. and Delzenne, N.M., 1998. Dietary fructans. *Annual Review of Nutrition*, 18(1), 117–143.
152. Nguyen T.D., Le Hoang, T., Nguyen T.L., Pham T.B., Tran T.H.H., Chau V.M. and Nguyen H.D., 2013. Inhibitors of a-glucosidase, a-amylase and lipase from *Chrysanthemum morifolium*, 54(1), 74–77.
153. Shimoda, H., Ninomiya, K., Nishida, N., Yoshino, T., Morikawa, T., Matsuda, H. and Yoshikawa, M., 2003. Anti-hyperlipidemic sesquiterpenes and new sesquiterpene glycosides from the leaves of artichoke (*Cynara scolymus* L.): Structure requirement and mode of action. *Bioorganic & Medicinal Chemistry Letters*, 13(2), 223–228.
154. Villiger, A., Sala, F., Suter, A. and Butterweck, V., 2015. In vitro inhibitory potential of *Cynara scolymus*, *Silybum marianum*, *Taraxacum officinale*, and *Peumus boldus* on key enzymes relevant to metabolic syndrome. *Phytomedicine*, 22(1), 138–144.
155. Rondanelli, M., Opizzi, A., Faliva, M., Sala, P., Perna, S., Riva, A., Morazzoni, P., Bombardelli, E. and Giacosa, A., 2014. Metabolic management in overweight subjects with naive impaired fasting glycaemia by means of a highly standardized extract from *Cynara scolymus*: A double-blind, placebo-controlled, randomized clinical trial. *Phytotherapy Research*, 28(1), 33–41.

156. Ooi, K.L., Muhammad, T.S.T., Tan, M.L. and Sulaiman, S.F., 2011. Cytotoxic, apoptotic and anti-α-glucosidase activities of 3, 4-di-O-caffeoyl quinic acid, an antioxidant isolated from the polyphenolic-rich extract of *Elephantopus mollis* Kunth. *Journal of Ethnopharmacology*, 135(3), 685–695.
157. Arsiningtyas, I.S., Gunawan-Puteri, M.D., Kato, E. and Kawabata, J., 2014. Identification of α-glucosidase inhibitors from the leaves of *Pluchea indica* (L.) Less., a traditional Indonesian herb: Promotion of natural product use. *Natural Product Research*, 28(17), 1350–1353.
158. Villiger, A., Sala, F., Suter, A. and Butterweck, V., 2015. In vitro inhibitory potential of *Cynara scolymus*, *Silybum marianum*, *Taraxacum officinale*, and *Peumus boldus* on key enzymes relevant to metabolic syndrome. *Phytomedicine*, 22(1), 138–144.
159. Huseini, H.F., Larijani, B., Heshmat, R.A., Fakhrzadeh, H., Radjabipour, B., Toliat, T. and Raza, M., 2006. The efficacy of *Silybum marianum* (L.) Gaertn.(silymarin) in the treatment of type II diabetes: A randomized, double-blind, placebo-controlled, clinical trial. *Phytotherapy Research*, 20(12), 1036–1039.
160. Ekanem, A.P., Wang, M., Simon, J.E. and Moreno, D.A., 2007. Antiobesity properties of two African plants (*Afromomum meleguetta* and *Spilanthes acmella*) by pancreatic lipase inhibition. *Phytotherapy Research*, 21(12), 1253–1255.
161. Prachayasittikul, V., Prachayasittikul, S., Ruchirawat, S. and Prachayasittikul, V., 2013. High therapeutic potential of *Spilanthes acmella*: A review. *EXCLI Journal*, 12, 291.
162. Ramsewak, R.S., Erickson, A.J. and Nair, M.G., 1999. Bioactive N-isobutylamides from the flower buds of *Spilanthes acmella*. *Phytochemistry*, 51(6), 729–732.
163. Zhang, J., Kang, M.J., Kim, M.J., Kim, M.E., Song, J.H., Lee, Y.M. and Kim, J.I., 2008. Pancreatic lipase inhibitory activity of *Taraxacum officinale* in vitro and in vivo. *Nutrition Research and Practice*, 2(4), 200–203.
164. Williams, C.A., Goldstone, F. and Greenham, J., 1996. Flavonoids, cinnamic acids and coumarins from the different tissues and medicinal preparations of *Taraxacum officinale*. *Phytochemistry*, 42(1), 121–127.
165. Schütz, K., Carle, R. and Schieber, A., 2006. Taraxacum—a review on its phytochemical and pharmacological profile. *Journal of Ethnopharmacology*, 107(3), 313–323.
166. Gao, H., Huang, Y.N., Gao, B., Xu, P.Y., Inagaki, C. and Kawabata, J., 2008. α-Glucosidase inhibitory effect by the flower buds of *Tussilago farfara* L. *Food Chemistry*, 106(3), 1195–1201.
167. Park, H.R., Yoo, M.Y., Seo, J.H., Kim, I.S., Kim, N.Y., Kang, J.Y., Cui, L., Lee, C.S., Lee, C.H. and Lee, H.S., 2008. Sesquiterpenoids isolated from the flower buds of *Tussilago farfara* L. inhibit diacylglycerol acyltransferase. *Journal of Agricultural and Food Chemistry*, 56(22), 10493–10497.
168. Culvenor, C.C.J., Edgar, J.A., Smith, L.W. and Hirono, I., 1976. The occurrence of senkirkine in *Tussilago farfara*. *Australian Journal of Chemistry*, 29(1), 229–230.
169. Leung, W.Y., Thomas, G.N., Chan, J.C. and Tomlinson, B., 2003. Weight management and current options in pharmacotherapy: Orlistat and sibutramine. *Clinical Therapeutics*, 25(1), 58–80.
170. Lee, I.A., Lee, J.H., Baek, N.I. and Kim, D.H., 2005. Antihyperlipidemic effect of crocin isolated from the fructus of *Gardenia jasminoides* and its metabolite crocetin. *Biological and Pharmaceutical Bulletin*, 28(11), 2106–2110.
171. Sheng, L., Qian, Z., Zheng, S. and Xi, L., 2006. Mechanism of hypolipidemic effect of crocin in rats: Crocin inhibits pancreatic lipase. *European Journal of Pharmacology*, 543(1), 116–122.
172. Wang, Z.W., Wang, J.S., Luo, J. and Kong, L.Y., 2013. α-glucosidase inhibitory triterpenoids from the stem barks of *Uncaria laevigata*. *Fitoterapia*, 90, 30–37.
173. Wan, L.S., Min, Q.X., Wang, Y.L., Yue, Y.D. and Chen, J.C., 2013. Xanthone glycoside constituents of *Swertia kouitchensis* with α-glucosidase inhibitory activity. *Journal of Natural Products*, 76(7), 1248–1253.
174. Wan, L.S., Chen, C.P., Xiao, Z.Q., Wang, Y.L., Min, Q.X., Yue, Y. and Chen, J., 2013. In vitro and in vivo anti-diabetic activity of *Swertia kouitchensis* extract. *Journal of Ethnopharmacology*, 147(3), 622–630.
175. Mir, S.R., Ahamad, J., Hassan, N. and Amin, S., 2014. Management of post prandial hyperglycemia with swertiamarin isolated from *Enicostemma littorale* Blume. *Planta Medica*, 80(10), PG13.
176. Arai, H., Hirasawa, Y., Rahman, A., Kusumawati, I., Zaini, N.C., Sato, S., Aoyama, C., Takeo, J. and Morita, H., 2010. Alstiphyllanines E–H, picraline and ajmaline-type alkaloids from *Alstonia macrophylla* inhibiting sodium glucose cotransporter. *Bioorganic & Medicinal Chemistry*, 18(6), 2152–2158.
177. Elya, B., Basah, K., Mun'im, A., Yuliastuti, W., Bangun, A. and Septiana, E.K., 2011. Screening of α-glucosidase inhibitory activity from some plants of *Apocynaceae*, *Clusiaceae*, *Euphorbiaceae*, and *Rubiaceae*. *BioMed Research International*, 2012, 6.
178. Begum, S., Syed, S.A., Siddiqui, B.S., Sattar, S.A. and Choudhary, M.I., 2013. Carandinol: First isohopane triterpene from the leaves of *Carissa carandas* L. and its cytotoxicity against cancer cell lines. *Phytochemistry Letters*, 6(1), 91–95.

179. Reddy, R.M.I., Latha, P.B., Vijaya, T. and Rao, D.S., 2012. The saponin-rich fraction of a *Gymnema sylvestre* R. Br. aqueous leaf extract reduces cafeteria and high-fat diet-induced obesity. *Zeitschrift Für Naturforschung C*, 67(1–2), 39–46.
180. Wang, Y., Dawid, C., Kottra, G., Daniel, H. and Hofmann, T., 2014. Gymnemic acids inhibit sodium-dependent glucose transporter 1. *Journal of Agricultural and Food Chemistry*, 62(25), 5925–5931.
181. Baskaran, K., Ahamath, B.K., Shanmugasundaram, K.R. and Shanmugasundaram, E.R.B., 1990. Antidiabetic effect of a leaf extract from *Gymnema sylvestre* in non-insulin-dependent diabetes mellitus patients. *Journal of Ethnopharmacology*, 30(3), 295–305.
182. Ali, K.M., Chatterjee, K., De, D., Jana, K., Bera, T.K. and Ghosh, D., 2011. Inhibitory effect of hydro-methanolic extract of seed of *Holarrhena antidysenterica* on alpha-glucosidase activity and postprandial blood glucose level in normoglycemic rat. *Journal of Ethnopharmacology*, 135(1), 194–196.
183. Kusano, S., 2000. Antidiabetic activity of white skinned sweet potato (*Ipomoea batatas* L.) in obese zucker fatty rats. *Biological and Pharmaceutical Bulletin*, 23(1), 23–26.
184. Ludvik, B., Neuffer, B. and Pacini, G., 2004. Efficacy of *Ipomoea batatas* (Caiapo) on diabetes control in type 2 diabetic subjects treated with diet. *Diabetes Care*, 27(2), 436–440.
185. Matsui, T., Ebuchi, S., Kobayashi, M., Fukui, K., Sugita, K., Terahara, N. and Matsumoto, K., 2002. Anti-hyperglycemic effect of diacylated anthocyanin derived from *Ipomoea batatas* cultivar Ayamurasaki can be achieved through the α-glucosidase inhibitory action. *Journal of Agricultural and Food Chemistry*, 50(25), 7244–7248.
186. Malalavidhane, T.S., Wickramasinghe, S.N. and Jansz, E.R., 2000. Oral hypoglycaemic activity of *Ipomoea aquatica*. *Journal of Ethnopharmacology*, 72(1), 293–298.
187. Malalavidhane, T.S., Wickramasinghe, S.M.D.N., Perera, M.S.A. and Jansz, E.R., 2003. Oral hypoglycaemic activity of *Ipomoea aquatica* in streptozotocin-induced, diabetic wistar rats and type II diabetics. *Phytotherapy Research*, 17(9), 1098–1100.
188. Sokeng, S.D., Rokeya, B., Hannan, J.M.A., Junaida, K., Zitech, P., Ali, L., Ngounou, G., Lontsi, D. and Kamtchouing, P., 2007. Inhibitory effect of *Ipomoea aquatica* extracts on glucose absorption using a perfused rat intestinal preparation. *Fitoterapia*, 78(7), 526–529.
189. Charnock, J.S., 2000. Gamma-linolenic acid provides additional protection against ventricular fibrillation in aged rats fed linoleic acid rich diets. *Prostaglandins, Leukotrienes and Essential Fatty Acids* (*PLEFA*), 62(2), 129–134.
190. Kavanagh, K., Flynn, D.M., Jenkins, K.A., Wilson, M.D. and Chilton, F.H., 2013. Stearidonic and γ-linolenic acids in Echium oil improves glucose disposal in insulin resistant monkeys. *Prostaglandins, Leukotrienes and Essential Fatty Acids* (*PLEFA*), 89(1), 39–45.
191. Horrobin, D.F., 1993. Fatty acid metabolism in health and disease: The role of delta-6-desaturase. *The American Journal of Clinical Nutrition*, 57(5), 732S–736S.
192. Murugesh, K., Yeligar, V., Dash, D.K., Sengupta, P., Maiti, B.C. and Maity, T.K., 2006. Antidiabetic, antioxidant and antihyperlipidemic status of *Heliotropium zeylanicum* extract on streptozotocin-induced diabetes in rats. *Biological and Pharmaceutical Bulletin*, 29(11), 2202–2205.
193. Schoental, R. and FRAYN, K.N., 1976. The effects of the pyrrolizidine alkaloid, heliotrine, and nicotinamide on the concentration of plasma insulin and blood glucose in the rat.
194. An, S., Park, Y.D., Paik, Y.K., Jeong, T.S. and Lee, W.S., 2007. Human ACAT inhibitory effects of shikonin derivatives from *Lithospermum erythrorhizon*. *Bioorganic & Medicinal Chemistry Letters*, 17(4), 1112–1116.
195. Accad, M., Smith, S.J., Newland, D.L., Sanan, D.A., King, L.E., Linton, M.F., Fazio, S. and Farese, R.V., 2000. Massive xanthomatosis and altered composition of atherosclerotic lesions in hyperlipidemic mice lacking acyl CoA: Cholesterol acyltransferase 1. *The Journal of Clinical Investigation*, 105(6), 711–719.
196. Komaki, E., Yamaguchi, S., Isafumi, M.A.R.U., Kinoshita, M., Kakehi, K. and Tsukada, Y., 2003. Identification of anti-α-amylase components from olive leaf extracts. *Food Science and Technology Research*, 9(1), 35–39.
197. Aparna, P., Tiwari, A.K., Srinivas, P., Ali, A.Z., Anuradha, V. and Rao, J.M., 2009. Dolichandroside A, a new α-glucosidase inhibitor and DPPH free-radical Scavenger from *Dolichandrone falcata* seem. *Phytotherapy Research*, 23(4), 591–596.
198. Tadera, K., Minami, Y., Takamatsu, K. and Matsuoka, T., 2006. Inhibition of α-glucosidase and α-amylase by flavonoids. *Journal of Nutritional Science and Vitaminology*, 52(2), 149–153.
199. Rani, M.P., Raghu, K.G., Nair, M.S. and Padmakumari, K.P., 2014. Isolation and identification of α-glucosidase and protein glycation inhibitors from *Stereospermum colais*. *Applied Biochemistry and Biotechnology*, 173(4), 946–956.

200. Dat, N.T., Dang, N.H. and Thanh, L.N., 2016. New flavonoid and pentacyclic triterpene from *Sesamum indicum* leaves. *Natural Product Research*, 30(3), 311–315.
201. Gao, H., Huang, Y.N., Gao, B., Li, P., Inagaki, C. and Kawabata, J., 2008. Inhibitory effect on α-glucosidase by *Adhatoda vasica* Nees. *Food Chemistry*, 108(3), 965–972.
202. Liu, Q., Hu, H.J., Li, P.F., Yang, Y.B., Wu, L.H., Chou, G.X. and Wang, Z.T., 2014. Diterpenoids and phenylethanoid glycosides from the roots of *Clerodendrum bungei* and their inhibitory effects against angiotensin converting enzyme and α-glucosidase. *Phytochemistry*, 103, 196–202.
203. Iqbal, K., Malik, A., Mukhtar, N., Anis, I., Khan, S.N. and Choudhary, M.I., 2004. α-Glucosidase inhibitory constituents from *Duranta repens*. *Chemical and Pharmaceutical Bulletin*, 52(7), 785–789.
204. Ayinampudi, S.R., Domala, R., Merugu, R., Bathula, S. and Janaswamy, M.R., 2012. New icetexane diterpenes with intestinal α-glucosidase inhibitory and free-radical scavenging activity isolated from *Premna tomentosa* roots. *Fitoterapia*, 83(1), 88–92.
205. Ramachandran, S. and Rajasekaran, A., 2014. Blood glucose-lowering effect of *Tectona grandis* flowers in type 2 diabetic rats: A study on identification of active constituents and mechanisms for antidiabetic action. *Journal of Diabetes*, 6(5), 427–437.
206. Singh, P.P., Jha, S. and Irchhaiya, R., 2012. Antidiabetic and antioxidant activity of hydroxycinnamic acids from *Calamintha officinalis* Moench. *Medicinal Chemistry Research*, 21(8), 1717–1721.
207. Jabeen, B., Riaz, N., Saleem, M., Naveed, M.A., Ashraf, M., Alam, U., Rafiq, H.M., Tareen, R.B. and Jabbar, A., 2013. Isolation of natural compounds from *Phlomis stewartii* showing α-glucosidase inhibitory activity. *Phytochemistry*, 96, 443–448.
208. Ma, H.Y., Gao, H.Y., Sun, L., Huang, J., Xu, X.M. and Wu, L.J., 2011. Constituents with α-glucosidase and advanced glycation end-product formation inhibitory activities from *Salvia miltiorrhiza* Bge. *Journal of Natural Medicines*, 65(1), 37–42.
209. Matsuura, H., Miyazaki, H., Asakawa, C., Amano, M., Yoshihara, T. and Mizutani, J., 2004. Isolation of α-glusosidase inhibitors from hyssop (*Hyssopus officinalis*). *Phytochemistry*, 65(1), 91–97.
210. Rizza, R.A., Gerich, J.E., Haymond, M.W., Westland, R.E., Hall, L.D., Clemens, A.H. and Service, F.J., 1980. Control of blood sugar in insulin-dependent diabetes: Comparison of an artificial endocrine pancreas, continuous subcutaneous insulin infusion, and intensified conventional insulin therapy. *New England Journal of Medicine*, 303(23), 1313–1318.
211. Heacock, P.M., Hertzler, S.R., Williams, J.A. and Wolf, B.W., 2005. Effects of a medical food containing an herbal α-glucosidase inhibitor on postprandial glycemia and insulinemia in healthy adults. *Journal of the American Dietetic Association*, 105(1), 65–71.
212. El-Beshbishy, H.A. and Bahashwan, S.A., 2012. Hypoglycemic effect of basil (*Ocimum basilicum*) aqueous extract is mediated through inhibition of α-glucosidase and α-amylase activities: An in vitro study. *Toxicology and Industrial Health*, 28(1), 42–50.
213. Baser, K.H.C., Kirimer, N. and Tümen, G., 1993. Composition of the essential oil of *Origanum majorana* L. from Turkey. *Journal of Essential Oil Research*, 5(5), 577–579.
214. Yamada, K., Murata, T., Kobayashi, K., Miyase, T. and Yoshizaki, F., 2010. A lipase inhibitor monoterpene and monoterpene glycosides from *Monarda punctata*. *Phytochemistry*, 71(16), 1884–1891.
215. Kawabata, J., Mizuhata, K., Nishioka, T., Aoyama, Y. and Kasai, T., 2003. 6-Hydroxyflavonoids as α-glucosidase inhibitors from marjoram (*Origanum majorana*) leaves. *Bioscience, Biotechnology, and Biochemistry*, 67(2), 445–447.
216. Damsud, T., Grace, M.H., Adisakwattana, S. and Phuwapraisirisan, P., 2014. Orthosiphol A from the aerial parts of *Orthosiphon aristatus* is putatively responsible for hypoglycemic effect via alpha-glucosidase inhibition. *Natural Product Communications*, 9(5), 639–641.
217. Ninomiya, K., Matsuda, H., Shimoda, H., Nishida, N., Kasajima, N., Yoshino, T., Morikawa, T. and Yoshikawa, M., 2004. Carnosic acid, a new class of lipid absorption inhibitor from sage. *Bioorganic & Medicinal Chemistry Letters*, 14(8), 1943–1946.
218. Vaquero, M.R., Yáñez-Gascón, M.J., Villalba, R.G., Larrosa, M., Fromentin, E., Ibarra, A., Roller, M., Tomás-Barberán, F., de Gea, J.C.E. and García-Conesa, M.T., 2012. Inhibition of gastric lipase as a mechanism for body weight and plasma lipids reduction in Zucker rats fed a rosemary extract rich in carnosic acid. *PLoS One*, 7(6), e39773.
219. Zhao, Y., Sedighi, R., Wang, P., Chen, H., Zhu, Y. and Sang, S., 2015. Carnosic acid as a major bioactive component in rosemary extract ameliorates high-fat-diet-induced obesity and metabolic syndrome in mice. *Journal of Agricultural and Food Chemistry*, 63(19), 4843–4852.
220. Ma, H.Y., Gao, H.Y., Sun, L., Huang, J., Xu, X.M. and Wu, L.J., 2011. Constituents with α-glucosidase and advanced glycation end-product formation inhibitory activities from *Salvia miltiorrhiza* Bge. *Journal of Natural Medicines*, 65(1), 37–42.

221. Kianbakht, S. and Dabaghian, F.H., 2013. Improved glycemic control and lipid profile in hyperlipidemic type 2 diabetic patients consuming *Salvia officinalis* L. leaf extract: A randomized placebo. Controlled clinical trial. *Complementary Therapies in Medicine*, 21(5), 441–446.
222. Ninomiya, K., Matsuda, H., Shimoda, H., Nishida, N., Kasajima, N., Yoshino, T., Morikawa, T. and Yoshikawa, M., 2004. Carnosic acid, a new class of lipid absorption inhibitor from sage. *Bioorganic & Medicinal Chemistry Letters*, 14(8), 1943–1946.
223. Asghari, B., Salehi, P., Sonboli, A. and Ebrahimi, S.N., 2015. Flavonoids from *Salvia chloroleuca* with α-amylsae and α-glucosidase inhibitory effect. *Iranian Journal of Pharmaceutical Research: IJPR*, 14(2), 609.
224. Nishioka, T., Kawabata, J. and Aoyama, Y., 1998. Baicalein, an α-glucosidase inhibitor from *Scutellaria baicalensis*. *Journal of Natural Products*, 61(11), 1413–1415.
225. Shimura, S., Tsuzuki, W., Kobayashi, S. and Suzuki, T., 1992. Inhibitory effect on lipase activity of extracts from medicinal herbs. *Bioscience, Biotechnology, and Biochemistry*, 56(9), 1478–1479.
226. Visavadiya, N.P. and Narasimhacharya, A.V.R.L., 2007. Ameliorative effect of Chlorophytum borivilianum root on lipid metabolism in hyperlipaemic rats. *Clinical and Experimental Pharmacology and Physiology*, 34(3), 244–249.
227. Thakur, G.S., Bag, M., Sanodiya, B.S., Debnath, M., Zacharia, A., Bhadauriya, P., Prasad, G.B.K.S. and Bisen, P.S., 2009. *Chlorophytum borivilianum*: A white gold for biopharmaceuticals and neutraceuticals. *Current Pharmaceutical Biotechnology*, 10(7), 650–666.
228. Lu, Y., Kuang, M., Hu, G.P., Wu, R.B., Wang, J., Liu, L. and Lin, Y.C., 2014. Loddigesiinols G–J: α-glucosidase inhibitors from *Dendrobium loddigesii*. *Molecules*, 19(6), 8544–8555.
229. Ghosh, S., More, P., Derle, A., Patil, A.B., Markad, P., Asok, A., Kumbhar, N., Shaikh, M.L., Ramanamurthy, B., Shinde, V.S. and Dhavale, D.D., 2014. Diosgenin from *Dioscorea bulbifera*: Novel hit for treatment of type II diabetes mellitus with inhibitory activity against α-amylase and α-glucosidase. *PLoS One*, 9(9), e106039.
230. Yang, M.H., Chin, Y.W., Yoon, K.D. and Kim, J., 2014. Phenolic compounds with pancreatic lipase inhibitory activity from Korean yam (*Dioscorea opposita*). *Journal of Enzyme Inhibition and Medicinal Chemistry*, 29(1), 1–6.
231. Shin, J.E., Han, M.J. and Kim, D.H., 2003. 3-Methylethergalangin isolated from *Alpinia officinarum* inhibits pancreatic lipase. *Biological and Pharmaceutical Bulletin*, 26(6), 854–857.
232. Shin, J.E., Han, M.J., Song, M.C., Baek, N.I. and Kim, D.H., 2004. 5-Hydroxy-7-(4′-hydroxy-3′-methoxyphenyl)-1-phenyl-3-heptanone: A pancreatic lipase inhibitor isolated from *Alpinia officinarum*. *Biological and Pharmaceutical Bulletin*, 27(1), 138–140.
233. Lin, L.Y., Peng, C.C., Yeh, Y.Y., Huang, B.Y., Wang, H.E., Chen, K.C. and Peng, R.Y., 2015. Antihyperlipidemic bioactivity of *Alpinia officinarum* (Hance) farw zingiberaceae can be attributed to the coexistance of curcumin, polyphenolics, dietary fibers and phytosterols. *Food & Function*, 6(5), 1600–1610.
234. Kenchaiah, S., Evans, J.C., Levy, D., Wilson, P.W., Benjamin, E.J., Larson, M.G., Kannel, W.B. and Vasan, R.S., 2002. Obesity and the risk of heart failure. *New England Journal of Medicine*, 347(5), 305–313.
235. Du, Z.Y., Liu, R.R., Shao, W.Y., Mao, X.P., Ma, L., Gu, L.Q., Huang, Z.S. and Chan, A.S., 2006. α-Glucosidase inhibition of natural curcuminoids and curcumin analogs. *European Journal of Medicinal Chemistry*, 41(2), 213–218.
236. Reddy, P.P., Tiwari, A.K., Rao, R.R., Madhusudhana, K., Rao, V.R.S., Ali, A.Z., Babu, K.S. and Rao, J.M., 2009. New Labdane diterpenes as intestinal α-glucosidase inhibitor from antihyperglycemic extract of *Hedychium spicatum* (Ham. Ex Smith) rhizomes. *Bioorganic & Medicinal Chemistry Letters*, 19(9), 2562–2565.
237. Shimada, T., Horikawa, T., Ikeya, Y., Matsuo, H., Kinoshita, K., Taguchi, T., Ichinose, K., Takahashi, K. and Aburada, M., 2011. Preventive effect of *Kaempferia parviflora* ethyl acetate extract and its major components polymethoxyflavonoid on metabolic diseases. *Fitoterapia*, 82(8), 1272–1278.
238. Akase, T., Shimada, T., Terabayashi, S., Ikeya, Y., Sanada, H. and Aburada, M., 2011. Antiobesity effects of *Kaempferia parviflora* in spontaneously obese type II diabetic mice. *Journal of Natural Medicines*, 65(1), 73–80.
239. Kim, H.S., Kim, Y.H., Hong, Y.S., Paek, N.S., Lee, H.S., Kim, T.M., Kim, K.W. and Lee, J.J., 1999. α-Glucosidase inhibitors from *Commelina communis*. *Planta Medica*, 65(05), 437–439.
240. Youn, J.Y., Park, H.Y. and Cho, K.H., 2004. Anti-hyperglycemic activity of *Commelina communis* L.: Inhibition of α-glucosidase. *Diabetes Research and Clinical Practice*, 66, S149–S155.
241. Asano, N., Oseki, K., Kizu, H. and Matsui, K., 1994. Nitrogen-in-the-ring pyranoses and furanoses: Structural basis of inhibition of mammalian glycosidases. *Journal of Medicinal Chemistry*, 37(22), 3701–3706.

242. Kite, G.C., Fellows, L.E., Fleet, G.W., Liu, P.S., Scofield, A.M. and Smith, N.G., 1988. α-Homonojirimycin [2, 6-dideoxy-2, 6-imino-D-glycero-L-gulo-heptitol] from *Omphalea diandra* L.: Isolation and glucosidase inhibtion. *Tetrahedron Letters*, 29(49), 6483–6485.
243. Levitan, E.B., Song, Y., Ford, E.S. and Liu, S., 2004. Is nondiabetic hyperglycemia a risk factor for cardiovascular disease?: A meta-analysis of prospective studies. *Archives of Internal Medicine*, 164(19), 2147–2155.