Bioactives in Nutritional and Metabolic Disorders

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Edited by

Shanti Bhushan Mishra
and Shradhanjali Singh

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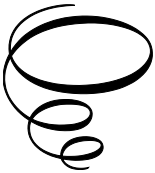

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FOREWORD

The book "Bioactives in Nutritional and Metabolic Disorders" offers readers comprehensive information for researching phytonutrients and secondary metabolites in metabolic disorders. Specifically, it delves into the treatment of these diseases through the utilization of biologically active compounds, as well as explores the crucial regulatory mechanisms of these bioactives in a variety of metabolic disorders. Additionally, the book critically evaluates phytonutrients as a potential source for novel drug candidate molecules. It is a compilation that presents the most up-to-date discoveries and insights in this field. The therapeutic potential of plant-derived nutrients and bioactives in managing various metabolic disorders is demonstrated in eleven informative chapters. Each chapter presents a detailed description of the main health alterations observed in each metabolic disorder, along with current figures and statistics from around the world. The authors also conduct thorough scientific background checks, providing a comprehensive analysis of all recommended phytochemicals for each disorder. Additionally, the mechanism (s) of action are described, and evidence from both in vivo and in vitro studies is included.

Chapter 1 – Comprehensive overview of metabolic disorders written by Aimen Salman discussed various metabolic disorders viz. Adrenoleukodystrophy, diabetes, Gaucher disease, glucose-galactose malabsorption, hereditary hemochromatosis, disorders related to carbohydrate lipid and protein metabolism, etc. Their pathophysiological conditions, diagnostic tests, and their treatments.

Chapter 2 – provides an overview of Hemochromatosis which is a condition characterized by excessive iron accumulation in the body. It also discussed various natural food supplements that may be beneficial for the treatment of Hemochromatosis.

Chapter 3 – Gaucher Disease is a genetic lysosomal storage disorder that is caused by mutations in the GBA gene affecting glucocerebrosidase enzyme activity. Within this chapter, its various types, symptoms, pathophysiology, and role of phytochemicals in the prevention of this disorder, have been reviewed.

Chapter 4 – The objective of this chapter was to analyze the role of therapeutic agents in preventing glucose-galactose malabsorption. This chapter covers the diagnosis, a general description of the disorder, current therapeutic approaches, etc. for preventing glucose-galactose malabsorption.

Chapter 5 – The main purpose of this chapter is to describe various approaches for preventing hepatitis with the help of phytocompounds and nutraceuticals. The chapter comprises pathophysiology, and various types of hepatitis and their treatment with the help of bioactive compounds.

Chapter 6 – Dyslipidemia, is a prevalent metabolic disorder characterized by abnormal lipid levels, and is associated with an elevated risk of cardiovascular diseases. The advent of functional foods, enriched with bioactive compounds and specific nutrients, has introduced a promising avenue for the management of dyslipidemia. The present chapter examines the intricate relationship between functional foods and dyslipidemia, exploring the mechanisms underlying their effects and evaluating the existing body of evidence supporting their role in lipid management.

Chapter 7 – The metabolic problem of type 2 diabetes mellitus (T2DM) is characterized by hyperglycemia and glucose intolerance. Cell reinforcement and anti-inflammatory effects can be had by bioactives, such as polyphenols, nutrients, and carotenoids, found in vegetables and organic products. Suggestions from cell or animal models indicate that bioactives may have direct effects on reducing hyperglycemia and enhancing insulin secretion. The possible hidden sub-molecular systems are described in this chapter.

Chapter 8 – The use of herbal supplements in phenylketonuria (PKU) therapy is gaining popularity among healthcare professionals. This chapter discusses the historical context of herbal medicine, investigates current research trends in PKU and herbal supplementation, and assesses probable processes and benefits. Safety factors, including risks and interactions, are thoroughly reviewed.

Chapter 9 – The purpose of the present chapter is to provide a comprehensive overview of the liver disorders induced by metabolic conditions associated with a sedentary lifestyle, increasing trend of intake of junk food and soft drinks, obesity, insulin resistance, and high blood lipids, which can cause oxidative stress, inflammation and excess fat storage in the liver, this condition is called nonalcoholic fatty liver disease (NAFLD) and the potential of phytochemicals in combating liver problems.

Chapter 10 – The present chapter explores the multifaceted roles of traditional Medicine systems and natural compounds in pancreatic cancer treatment, highlighting their potential as complementary therapies to conventional treatments.

Chapter 11 – Obesity is a chronic metabolic disorder that may arise due to an unhealthy diet, genetic predisposition, a sedentary lifestyle, and sometimes medicines. This chapter discusses the role of phytonutrients in combating obesity and the comorbidities associated with it.

Chapter 12 – Nutritional and metabolic disorders, encompassing conditions such as obesity, diabetes, and cardiovascular diseases, pose significant global health challenges. This chapter explores the emerging role of bioactives in managing and preventing these disorders. Bioactives are naturally occurring compounds found in food that exert beneficial effects on human health beyond basic nutritional functions. This chapter highlights the key bioactive compounds, including polyphenols, flavonoids, and omega-3 fatty acids, that have demonstrated potential in mitigating nutritional and metabolic disorders.

PREFACE

The journey towards wellness is often multifaceted and intricate in the realm of nutrition and metabolic disorders. This book, "Bioactives in Nutritional and Metabolic Disorders," emerges as a beacon illuminating the synergistic relationship between bioactive compounds and the intricate web of metabolic functions within the human body. Through its pages, readers will embark on an enlightening expedition through the latest research, insights, and applications of bioactives in combating a spectrum of metabolic disorders.

From the meticulous exploration of phytochemicals to the nuanced understanding of their mechanisms of action, each chapter unfolds a tapestry of knowledge, meticulously woven by esteemed experts in the field. Through their collective wisdom, this volume transcends conventional boundaries, delving into the realms of nutraceuticals, functional foods, and therapeutic interventions. The significance of this compendium extends beyond academia, resonating with clinicians, nutritionists, researchers, and individuals navigating the labyrinth of metabolic disorders. It serves as a cornerstone for informed decision-making, offering a roadmap towards holistic approaches to health and well-being. As the global community grapples with the burgeoning burden of metabolic disorders, the imperative for comprehensive solutions has never been more pressing. In this context, the elucidation of bioactives emerges as a pivotal paradigm, heralding a new dawn in personalized nutrition, preventive medicine, and therapeutic innovation. With humility and anticipation, we present "Bioactives in Nutritional and Metabolic Disorders" as a testament to the collective endeavor to unravel the mysteries of nature's pharmacopeia and harness its potential for the betterment of human health. May its insights inspire, its knowledge empowers, and its implications catalyze a transformative journey towards a healthier, more vibrant future.

Dr. Shanti Bhushan Mishra
Dr. Shradhanjali Singh

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Writing a book is often a collaborative effort, and this work is no exception. I am deeply grateful to those who have contributed to the creation of *Bioactives in Nutritional and Metabolic Disorders*.

First and foremost, I would like to express my sincere appreciation to my esteemed colleagues and experts in the fields of nutrition and metabolic disorders. Their insightful feedback, extensive knowledge, and unwavering support have been invaluable throughout this journey.

I am also thankful to the dedicated team at Cambridge Scholars Publishing for their professionalism and commitment to bringing this project to fruition. Their meticulous editing, design, and production efforts have significantly enhanced the quality of the final product.

To my research assistants and students who helped gather and analyze data, your hard work and enthusiasm were critical in compiling the latest research and case studies included in these chapters.

I would also like to acknowledge the support of my family and friends, who provided encouragement and understanding during the long hours spent working on this book. Your patience and belief in this project have been a constant source of motivation.

Finally, I dedicate this book to the readers and practitioners in the field, whose dedication to advancing knowledge in nutrition and metabolic health inspires us all. I hope that this work will contribute to your understanding and efforts in addressing these complex disorders.

Thank you to everyone who played a role in making this book a reality.

With gratitude,
Dr. Shanti Bhushan Mishra
Dr. Shradhanjali Singh

ABBREVIATIONS

AA	Amino acid
AD	Autosomal dominant
AgRP	Agouti-related protein
AR	Autosomal recessive
BAT	Brown adipose tissue
CAD	Coronary Artery Disease
CART	Cocaine and amphetamine-related transit
CGRP	Calcitonin gene-related protein
CNS	Central nervous system
CPDD	Calcium Pyrophosphate Deposition Disease
CYP450	Cytochrome P450
C/EBPβ	CCAAT/enhancer binding protein beta
DMTI	Divalent metal transporter 1
EDC	Endocrine disrupting chemicals
EMA	European Medicines Agency
FA	Fatty acid
FFA	Free fatty acids
GHS-R	Growth hormone secretagogue receptor
gm	Grams
GI	Gastrointestinal
HAMP	Hepcidin antimicrobial peptide
Hb	Haemoglobin
HC	Hemochromatosis
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus.
HFD	High-Fat Diet
HFE	Hereditary Haemochromatosis Type 1
HH	Hereditary hemochromatosis
HIV	Human Immuno Virus
HJV	Homojuvelin
HO-1	Hemooxygenase-1
HSL	Hormone-sensitive lipase
IO	Iron Overload
JAK	Janus kinases/signal transducers

LDL	Low-density lipoprotein
LEPR	Leptin Receptors
LIC	Liver Iron Content
MAPKs	Mitogen-Activated Protein Kinases
MCP	Metacarpophalangeal
MCP-1	Monocyte chemo-attractant protein-1
MOA	Mechanism of action
MRI	Magnetic resonance imaging
MSCs	Mesenchymal Stem Cells
Muc2	Mucin 2 Gene
NTBI	Non-transferrin bund iron
NAFLD	Nonalcoholic Fatty Liver Disease
PACC	Phosphorylated acetyl-CoA carboxylase
Pgc-1α	Peroxisome proliferator-activated receptor gamma coactivator 1-alpha
POMC	Pro-opiomelanocortin
PPIs	Proton pump inhibitors
Prdm16	PR Domain-Containing16
ROS	Reactive oxygen species
RH	Related Haemochromatosis
Scd1	Stearoyl-CoA desaturase-1
SF	Serum ferritin
SH2	Src homology 2
STAT	Signal transducer and activator of transcription
TF	Transferrin
TNF-α	Tumor necrosis factor-alpha
TSAT	Transferrin Saturation
TSAT	Transferrin-Iron Saturation
TfR2	Transferrin receptor 2
UCP1	Uncoupling protein 1
WAT	White adipose tissue
WHO	World Health Organization
↓	Decrease
↑	Increase
α	Alpha
β	Beta
γ	Gamma
ε	Epsilon

CHAPTER 1

COMPREHENSIVE OVERVIEW OF METABOLIC DISORDERS

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Abstract

Thousands of systems operate beneath the surface to maintain optimal health. Our metabolism is one of the most important components of the jigsaw. From maintaining blood circulation to aiding in food digestion, metabolism is involved in many body processes. A metabolic disease, which occurs when aberrant chemical interactions impair the metabolic process, affects normal metabolic function in certain individuals. Non-communicable illnesses now have a very high global burden. The majority of these are referred to as "metabolic disorders." These conditions might exist from birth or could arise later. People of all ages can be impacted by metabolic diseases, which often have detrimental consequences on the nervous system and cardiovascular systems. Nearly 1-3 percent of children worldwide suffer from metabolic abnormalities, according to a recent World Health Organisation report. According to recent epidemiological research conducted by the Centres for Disease Control and Prevention (CDC), metabolic diseases affect 10% of adult Americans. These illnesses eventually develop into chronic conditions that are challenging to treat, even with medical assistance.

Keywords: Centres for Disease Control and Prevention, health, metabolic diseases, epidemiological

1. Introduction

Originally, metabolic disorder was more of a theory than a medical diagnosis. In 1920, Swedish physician Kylin established a link between hypertension, hyperglycemia, and gout. This finding led to the development of the metabolic syndrome (Cleeman 2001). Later in 1947, Vague wrote on the widespread correlation between visceral obesity and the metabolic anomalies present in Type 2 Diabetes Mellitus and Cardiovascular Disease. After that, in 1965, Avogaro and Crepaldi published an abstract at the annual conference of the European Association for the Study of Diabetes, which once more detailed a syndrome consisting of obesity, hyperglycemia, and hypertension. In the wake of Reaven's 1988 Banting Lecture, the field made considerable progress (Einhorn 2003). He coined the term "Syndrome X" to refer to "a cluster of risk factors for diabetes and cardiovascular disease." His introduction of the idea of insulin resistance was his principal contribution. Surprisingly, though, he left out obesity, or visceral obesity, from the definition, which was subsequently included as a vital abnormality (Group 2005). For the combination of upper body obesity, glucose intolerance, hypertriglyceridemia, and hypertension, Kaplan dubbed the syndrome "The Deadly Quartet" in 1989. However, it was renamed "The Insulin Resistance Syndrome" once more in 1992. Several organizations have made an effort to create diagnostic standards for metabolic disorders. A World Health Organisation (WHO) diabetes panel made the initial effort to define the metabolic disorder in 1998. In 1999, the WHO definition was modified in retaliation by the European Group for the research on Insulin Resistance (EGIR) (Shaw *et al.,* 2003). The definition was published by the National Cholesterol Education Programme Adult Treatment Panel (NCEP/ATP) in 2001. The American Association of Clinical Endocrinologists (AACE) then provided their opinions on the syndrome's description in 2003. The abundance of definitions implied the need for a single, cohesive definition. The International Diabetes Federation (IDF) put up a revised definition of the metabolic disorder in April 2005 with the intention of achieving this.

2. Metabolic Disorder

The phrase "metabolic disorder" describes a group of conditions that obstruct the body's normal metabolic processes. The two processes that comprise the typical metabolic process are anabolism, which produces complex molecules from simpler ones, and catabolism, which produces simpler molecules from complex ones. Any one of the two processes may alter as a result of certain chemical reactions in the body. These illnesses eventually lead to a metabolic block that causes dangerous substances to

build up throughout the body (Sm 1992). Primary metabolic illnesses are divided into two categories. Again, the body cannot suitably use this energy. This is the second prerequisite. Metabolic disorders can affect a few vital body organs. These are the pancreas, the liver, and the intestines. When metabolism is working properly, it distributes oxygen throughout the body and combines the calories you eat with energy. The metabolism converts nutrients from meals into fuel or stores them for later use by using hormones and enzymes. In addition to helping the body to develop, heal wounds, and regulate body temperature, a good diet also supports metabolic functions (Eckel *et al.,* 2005). Metabolic diseases are often caused by excess or deficiency of the chemicals necessary for normal metabolic activity. By interfering with one or more of the following "ingredients" of the metabolic process; lipids; carbohydrates; and amino acids, these illnesses affect metabolism. Other metabolic illnesses that impact cells' energy-producing components are referred to as mitochondrial diseases (Ford 2004). Thousands of enzymes participate in several interrelated metabolic pathways throughout these events. Among the essential biochemical processes that are hampered by metabolic diseases include the digestion or transport of proteins (amino acids), carbohydrates (sugars and starches), or lipids (fatty acids). These disorders are typically hereditary, even though the majority of persons with metabolic illnesses may not exhibit symptoms for days, months, or even years. Usually, when symptoms initially manifest, such as during a feverish illness or a prolonged fast, the body's metabolism is under stress. Prenatal diagnostic screening for some metabolic disorders can be achieved (Grundy *et al.,* 2005, Wilson *et al.,* 2005, Ritchie *et al.,* 2007).

This kind of testing is frequently available to families who are members of a certain ethnic group or who have had a kid with a metabolic problem in the past. For example, testing for Tay-Sachs disease is rather common among Ashkenazi Jews. In countries where metabolic disorders are evaluated from birth, a maximum of five issues might be examined. Tandem mass spectrometry is a novel technology that allows the identification of many abnormal metabolites almost simultaneously, expanding the range of disorders for which neonates may be examined by almost thirty. If a metabolic anomaly is found soon after delivery, an infant's prognosis can be improved with an early diagnosis and appropriate medicine. Treatment for some metabolic diseases can be initiated early and has a very positive response rate. Others, nevertheless, despite an early diagnosis, have no viable therapy and create serious issues. Gene therapy may work well in the future to treat some of these illnesses (Ford *et al.,* 2002). When seen together, metabolic illnesses are somewhat frequent, despite being extremely uncommon when diagnosed alone. The incidence of some metabolic

illnesses ranges from less than 1 in 1,000,000 to about 1 in 500 (or even higher among isolated groups). It is believed that 1 in 1,000 people are affected by metabolic diseases collectively.

3. Epidemiology

Globally, the prevalence of Metabolic Disorder ranges from less than 10% to 84%, depending on the region, urban or rural environment, age, sex, race, and ethnicity, as well as the particular diagnosis used. The International Diabetes Federation (IDF) estimates that 25% of adult people worldwide suffer from metabolic disorders. A greater body mass index (BMI), a sedentary lifestyle, and a higher socioeconomic status were all significantly associated with metabolic disorders. Several variables, such as differences in genetic background, diet, physical activity levels, smoking, family history of diabetes, and education, affect the occurrence of the metabolic illness and its components. In the National Health and Nutrition Examination Survey (NHANES), the metabolic disorder was shown to be more common in participants who were normal weight (5%), overweight (22%), and obese (60%) than in underweight patients. With increasing age, it rises to 10% for those in the 20–29 age range, 20% for those in the 40–49 age range, and 45% for those in the 60–69 age range. Worldwide, the prevalence of metabolic disorders ranged from 7% to 56% in women and from 8% to 43% in men, according to the NCEP-ATP III criteria, 2001 (Ponholzer *et al.,* 2008). The prevalence of metabolic syndrome rises for both males and females between the ages of 20 and the sixth and seventh decade of life, respectively. According to Ponholzer *et al.,* 2008, postmenopausal women have a high prevalence of metabolic disorders, ranging from 32.6% to 41.5%. According to a report from the Framingham Heart Study, gaining more than 2.25 kg over 16 years was linked to a 45% increased risk of Metabolic Disorder development. Furthermore, an increase in waist circumference (WC) of 11 cm is linked to an adjusted 80% greater chance of getting the syndrome within 5 years, according to research by Palaniappan *et al.,* 2004. The metabolic alterations occur more frequently than would be expected by chance, and the sum of the reasons increases the risk of cardiovascular disease beyond what would be expected from each cause alone. The risk increases with the number of metabolic disease components present (Reilly *et al.,* 2003, Palaniappan *et al.,* 2004).

4. Causes of metabolic disorders

The following is a list of the primary causes of metabolic disorders:

4.1 Infections

Dehydration, electrolyte imbalance, and acid-base imbalance can all result from infections brought on by a few viral pathogens. Once again, intestinal epithelial infections caused by certain bacterial agents, such as Escherichia coli, can cause the production of water and electrolytes. Diarrhoea, electrolyte imbalance, and dehydration result from this (Cinti 2005, Andreadis *et al.,* 2007, Halberg *et al.,* 2008).

4.2 Toxicity

Certain substances can cause gastrointestinal tract tissue damage, which can lead to secondary metabolic disorders. An example of this would be the disruption of cholinesterase enzyme activity caused by certain organophosphate chemicals (acetylcholine metabolism). Once more, a kind of fungal toxin called aflatoxin B1 can harm the liver acutely and potentially result in hepatic encephalopathy.

4.3 Drugs

Abuse of some medications may result in the suppression of vital enzymatic processes. For instance, excessive cortisone usage can block phospholipase A2 and cause Cushing's disease.

4.4 Hormone

An imbalance in hormones during menopause or pregnancy might cause problems with regular metabolic functions. These conditions include hyperparathyroidism (metabolic bone disease), Addison's disease (caused by an aldosterone insufficiency), and diabetes mellitus (caused by an insulin shortage).

4.5 Diet

Several vital minerals and vitamins co-factor with several enzymes involved in energy metabolism. Metabolic problems can arise from a typical diet lacking in certain nutrients.

4.6 Genetic factors

Several genetic abnormalities, primarily autosomal recessive syndromes, can result in incorrect synthesis or insufficient amounts of the enzymes needed for metabolic processes. The conditions that result in an insufficiency of the enzymes pyruvate kinase and phenylalanine hydroxylase are two notable instances of this group.

4.7 Organ problems or failures

Metabolic diseases can arise when organs involved in metabolism, such as the pancreas, liver, or kidneys, cease to operate normally. Internal organ problems can arise long after birth, and some are hereditary.

5. Pathophysiology

Chronic low-grade inflammation is a condition known as a metabolic disorder, which results from the intricate interaction of environmental and hereditary variables. Numerous factors contribute to the syndrome, such as endothelial dysfunction, high blood pressure, hypercoagulable condition, insulin resistance, visceral obesity, atherogenic dyslipidemia, hereditary susceptibility, and chronic stress (Cinti 2005). Some typical signs of metabolic diseases are hepatoencephalopathy, hypotonia, liver enlargement (hepatomegaly), vomiting and diarrhea, occasional convulsions, and seizures. The effects of metabolic disorders are shown in Table 1.1.

5.1 Types of Metabolic Disorders

There are many types of metabolic disorders as follows:

5.1.1 Adrenoleukodystrophy

Adrenoleukodystrophy (ALD)is a genetically based metabolic condition. The brain and adrenal cortex of the individuals have extended chains of fatty acids. The degradation of the myelin sheath on nerve fiber is brought on by the inhibition of the enzymes responsible for the disintegration of fatty acid chains. Death and neurological impairment are possible outcomes.

5.1.2 Diabetes

One of the most common metabolic illnesses, diabetes affects around 10% of the US population. Since insulin, the hormone impacted by diabetes is involved in the metabolic process, diabetes, despite being categorized as an

autoimmune illness, is a metabolic problem. Diabetes is of two types: Type 1 diabetes: This hereditary disorder prevents your pancreas from generating insulin. Type 2 diabetes: This more common kind of illness can be hereditary or develop as a result of not getting enough exercise or becoming overweight later in life. In type 2 diabetes, the body still produces insulin, but not as effectively (Lau *et al.,* 2005). The following are signs of diabetes: frequent urination; frequent sensations of thirst and hunger; blurred eyesight; dry skin; sores and infections that take longer to cure. Fortunately, diabetes may be treated in either form. Treatment for type 1 diabetes includes insulin pumps or injections. For type 2, it is advised to adopt a nutritious diet, engage in regular exercise, and occasionally take medication.

5.1.3 Gaucher disease

This type of hereditary illness is brought on by a gene mutation linked to the glucocerebrosidase enzyme, which breaks down a specific type of fat known as glucocerebroside. Individuals with this illness typically have an overabundance of fat deposited in their spleen, liver, and bone marrow. This illness may result in mortality, bone damage, and anemia. A genetic disorder known as Gaucher disease may only be passed on to children if both parents carry the defective gene. The symptoms of Gaucher disease include anemia (low red blood cell count), pain in the stomach, weak or painful bones, fatigue, frequent bruising, and nose bleeding. Most kinds of Gaucher illness are treatable. Treatment options that are often used include substrate reduction therapy (SRT) and enzyme replacement therapy (ERT). Whereas ERT is administered intravenously, SRT is taken orally.

5.1.4 Glucose-galactose malabsorption

The main feature of this metabolic disease is intolerance to galactose, lactose, sucrose, and glucose. The linings of the small intestine are not able to efficiently absorb glucose and galactose. This disorder is recessive. This disorder is caused by two faulty copies of the SGLT1 gene.

5.1.5 Hereditary hemochromatosis

An over absorption of iron from the intestines is the hallmark of this metabolic condition. As a result, the pancreas and liver, among other organs, have an overabundance of iron. Hemochromatosis is mostly caused by mutations in the HFE gene.

5.1.6 Lesch Nyhan syndrome

This genetic metabolic condition results from a malfunction in the metabolism of purines, which are essential building blocks of DNA and RNA. Purine production and recycling include several enzymes. This disorder is caused by mutations in the HPRT1 gene.

5.1.7 Maple syrup urinedisease (MSUD)

This condition is characterized by unusually sweet urine and is brought on by an insufficient metabolism of amino acids. Other symptoms of the condition include slowed development, odd movements, vomiting, lethargy, and, if untreated, seizures. Since MSUD patients have difficulty breaking down the amino acids valine, leucine, and isoleucine, the most common type of therapy is a lifelong diet plan that restricts the consumption of these essential nutrients. If left untreated, MSUD can result in a coma or, in the worst cases, even death (Lau *et al.,* 2005)**.**

5.1.8 Phenylketonuria

This metabolic condition is brought on by an insufficient amount of the enzyme phenylalanine hydroxylase. It may result in pregnancy difficulties, organ damage, and retardation (Trayhurn *et al.,* 2004). The following are common symptoms: odorous skin, breath, or urine; rashes or dermatitis regularly; hyperactivity; microcephaly (smaller head size); delayed development; behavioral problems. Similar to MSUD, the mainstay of treatment is to restrict meals that contain the offending amino acid, such as aspartame, and foods high in protein.

5.1.9 Lysosomal storage disease

This condition is typified by the partial breakdown of catabolic chemicals, which leads to their accumulation in the tissues. In this disorder, damage to the central nervous system develops (Lau *et al.* 2005).

5.1.10 Hunter syndrome

Hunter syndrome is a hereditary metabolic disorder that is considerably more frequent in males than in women. The metabolic syndrome is brought on by a missing or malfunctioning key enzyme. The following age range is when Hunter syndrome symptoms first appear: big head (macrocephaly); wide nose; full lips. Long-term diarrhoea; tight joints; delayed development; louder voice due to bigger vocal cords. These symptoms may cause

respiratory and cardiovascular issues. While there is no known treatment for Hunter syndrome, the symptoms can be controlled. For example, since sleep apnea is a common symptom, devices that keep the airway open while you sleep are often prescribed (Trayhurn and Wood 2004).

5.1.11 Tay-Sachs illness

Similar to multiple systems inherited diabetes, Tay-Sachs disease is a hereditary metabolic condition brought on by the incapacity to metabolize a chemical. On the other hand, Tay-Sachs patients lack an enzyme that aids in the digestion of fatty foods. Infantile Tay-Sachs disease is the most prevalent kind, with symptoms appearing between three and six months of age (Trayhurn and Wood 2004). The following are typical symptoms: impaired mobility; seizures; "cherry-red" patches in the eyes; difficulty swallowing; loss of hearing and vision; weakening in the muscles and problems with motor skills.

5.1.12 Juvenile or late-onset

Tay-Sachs disease can seldom affect children five years of age and older. In contrast to the infantile type, symptoms include behavioral issues and respiratory illnesses, weakened muscles; tremors or muscular spasms; mental decline; and psychiatric illnesses. Unfortunately, Tay-Sachs disease can deteriorate over time and is frequently deadly. Nonetheless, genetic screening assays are capable of identifying the disease-causing genes. You can obtain genetic testing and counseling before getting pregnant if there is a family history of the condition (Trayhurn and Wood 2004).

5.1.13 Wilson's illness

Wilson's disease is a genetic metabolic illness that causes the brain, liver, and other organs to accumulate copper. It is a hereditary condition that is inherited from parent to kid from birth. The body needs a particular quantity of copper to create neurons, bones, melanin, and collagen, even though most people don't think of copper as food. Normally, your body uses the copper in your food to make the appropriate amounts, sending the excess to your liver for excretion. A few distinct symptoms of Wilson's illness include jaundice, golden-brown staining of the eye, fluid accumulation in the legs or belly, fatigue, appetite loss, and stiffness in the muscles. Wilson's illness can be cured, even if too much copper can be fatal—especially if detected early. Treatment entails continuing to monitor symptoms and taking medicine for the rest of one's life (Saleem *et al.,* 2009).

Table 1.1 Systemic Effects of Metabolic Disorder

System	Metabolic Disorder
Renal	Chronic kidney disease, focal segmental glomerulosclerosis, glomerulomegaly, hemofiltration, hyperfiltration, and microalbuminuria (Tsimikas *et al.* 2009)
Hepatic	Elevated blood transaminase, cirrhosis, hepatic fibrosis, non-alcoholic fatty liver disease (NAFLD), and non-alcoholic steatohepatitis (NASH) (Jacobs *et al.* 2009)
Skin	Skin cancer, psoriasis, androgenetic alopecia, lichen planus, burn-induced insulin resistance, acanthosis nigricans, skin tags, and acne inversa
Ocular	Age-related cataracts (nuclear, cortical, posterior sub capsular), non-diabetic retinopathy, oculomotor nerve palsy, central retinal artery blockage, primary open-angle glaucoma, and lower lid entropion
Sleep	Obstructive sleep apnea (OSA)
Reproductive System	Polycystic ovarian syndrome (PCOS), hypogonadism, and erectile dysfunction
Cardiovascular System	Heart attacks, myocardial infarctions, and coronary heart disease (CHD)
Cancers	Breast, pancreas, and prostate

5.2 Main Diagnostic Tests

Certain laboratory tests must be performed to properly diagnose metabolic diseases including fasting glucose, total cholesterol count and LDL cholesterol count, Blood pressure, and Triglycerides.

5.3 Treatment and Prevention

5.3.1 Treatment for Adrenoleukodystrophy (ALD)

Bone marrow replacement surgery can be used to extract stem cells from the bone marrow. If ALD is detected early, this therapeutic approach can slow its development. Steroids may be used to treat adrenal insufficiency when the adrenal gland is unable to generate enough hormones. Physical therapy aids in easing muscular stiffness and spasms (Guldiken *et al.,* 2007). Early identification and treatment are necessary if the kid is born with ALD to stop the condition from getting worse.

5.3.2 Treatment for Gaucher's illness

The patient may require enzyme replacement therapy as part of their treatment for this illness. Intravenous artificial enzymes are used in this treatment. For patients with Gaucher's disease, medications are provided to lower their blood levels of fatty compounds. Gaucher's disease patients also receive osteoarthritis medication. Patients' bone density is increased by these drugs. If a person wishes to establish a family, they should obtain genetic counseling if they have Gaucher's disease or have a family history of the condition.

5.3.3 Treatment for Diabetes type 1

Insulin pens or injections are two ways that it can be given. An insulin pen and an ink pen have the same appearance. The patient can immediately inject this into their skin. Using an insulin pump is an additional technique for administering insulin. Patients with type 1 diabetes are prescribed medications to decrease blood pressure, and cholesterol, and preserve heart health. A tiny device is affixed to the exterior of the body, and a cable connected to it passes into the skin. Physical treatment is crucial for people with type 1 diabetes as it helps to maintain a stable blood pressure and blood sugar level. Patients with type 1 diabetes have their blood sugar levels checked. To assist make daily tasks simpler, people with type 1 diabetes can implement a few lifestyle modifications such as monitoring cholesterol, blood pressure, and blood sugar, giving up smoking, paying attention to their feet, retaining a balanced weight, eating wholesome, clean foods such as fruits, veggies, whole grains, etc, avoid consuming too much alcohol.

5.3.4 Treatment for lysosomal storage disorder

Individuals with a diagnosis of lysosomal storage disease are administered medications to restore missing enzymes. Doctors administer medications to get rid of the extra enzymes the body has accumulated. It is possible to obtain new stem cells following a bone marrow transplant. This therapeutic approach aids in mitigating the symptoms associated with lysosomal storage disease. There are no foolproof ways to avoid this illness.

5.4 Causes of metabolic disorders

5.4.1 Metabolic pathways

In 1908, the British physician Sir Archibald Garrod hypothesized that defects in specific biochemical processes, perhaps due to decreased activity or the absence of a certain enzyme might be the cause of four lifelong hereditary disorders: cystinuria, albinism, pentosuria, and alkaptonuria. He named these conditions "inborn errors of metabolism." Expanding upon this, it's fascinating to observe how Garrod's pioneering thoughts laid the groundwork for the field of genetics and metabolic diseases. He was among the first to connect the dots between genetics and biochemistry, suggesting that a genetic defect could lead to a malfunction in the metabolic process. This insight was groundbreaking at the time, paving the way for the development of modern genetics and our understanding of hereditary diseases. From his time onwards, the catalog of identified hereditary inborn errors of metabolism has seen significant expansion. This chapter focuses exclusively on genetic metabolic diseases, despite acknowledging that various other conditions, such as endocrine disorders (such as diabetes mellitus and hypothyroidism) and malnutrition issues (including marasmus and kwashiorkor), also influence cellular metabolism. In doing so, it highlights the crucial advances and ongoing research efforts aimed at understanding and managing these complex genetic conditions (McLaughlin *et al.,* 2002).

Cellular enzymes, which are proteins that catalyze the transformation of materials known as substrates into products with unique biochemical structures, break down food into many components. These products then serve as the substrate for the next enzyme in a metabolic pathway. Obstruction of a pathway, insufficient production of the finished product, or lack of or decreased activity of an enzyme causes illness. An inactive enzyme leads to the accumulation of its substrate, which can become dangerous if it accumulates in too great an amount. Additionally, the

accumulation of a substrate may activate tiny, ordinarily dormant metabolic pathways, resulting in the creation of novel and potentially hazardous metabolites.

Dozens of metabolic pathways exist in every cell of the body, and since they are all interconnected, a single blockage can affect a broad spectrum of biochemical functions. The malfunctioning of a specific enzyme can lead to a metabolic imbalance, causing severe side effects including intellectual disability, seizures, decreased muscle tone, organ failure, blindness, and deafness. Recently, it has become apparent that there is frequently a metabolic component to illnesses associated with various congenital defects, such as Smith-Lemli-Opitz syndrome (McLaughlin *et al.,* 2002).

5.4.2 Mutations in genes

The cell nucleus contains deoxyribonucleic acid (DNA), the molecular blueprint for nearly all enzymes, structural proteins, cellular transport proteins, and other components involved in complex metabolic processes. The cellular organelles called mitochondria also contain a small amount of DNA, essential for metabolism. Genes, small segments of DNA, regulate the production of certain proteins or enzymes. American geneticists George Beadle and Edward Tatum proposed the "one quality one compound" thought in 1945, which expresses that those-solitary quality controls the blend should be of a solitary chemical. The key idea of atomic science is this one. This idea has been improved to take into account the fact that not all enzymes are produced by genes and that some enzymes contain numerous structural elements that are encoded by multiple genes (PM 2003).

Nonetheless, the one quality, one protein hypothesis had clear ramifications when Garrod's initial speculations concerning characteristic mistakes of digestion were applied. It was once generally accepted that hereditary changes bringing about deficient compounds with reduced or missing exercises caused innate metabolic issues (Guldiken *et al.,* 2007). The first hereditary sickness in quite a while viewed as brought about by a lack of catalyst was methemoglobinuria in 1948. In 1949, it was discovered that the protein called hemoglobin, which is found in red blood cells and carries oxygen to the body's tissues, behaved differently when taken from healthy human red blood cells than it did when taken from people with sickle-cell anemia, a genetic condition. This revelation was made by American scientific expert Linus Pauling and partners. In this way, it was found that natural mistakes of digestion are brought about by freak qualities that

control the development of abnormal proteins with changed capabilities (PM 2003).

5.4.3 Inheritance

Inherent mistakes of digestion are generally acquired via autosomal passive legacy, implying that two broken qualities are expected to create the infection's side effects. Considering that half of ordinary catalyst movement is sufficient to keep up with fitting wellbeing, guardians of a kid with the condition are habitually transporters of the sickness with no side effects. Notwithstanding, when two transporters of a negative component have a youngster, there is a 25% gamble that the kid will be impacted, a 25% opportunity that the kid will not have the freak quality, and a half opportunity that the kid will likewise be a transporter. As far as hereditary qualities, a person with the condition is homozygous for having two freak qualities, while an autosomal latent problem transporter is heterozygous for having only one freak quality (Clearfield 2005). All human genomes contain approximately six recessive mutant alleles; however, it is uncommon for two individuals with distinct mutations in the same gene to mate. Be that as it may, because a common hereditary foundation exists in circumstances of parental relationship, there is a raised likelihood of considering a youngster with an autosomal latent problem (Pedersen *et al.,* 2003). Autosomal prevailing sicknesses, rather than autosomal latent illnesses, manifest when a solitary blemished quality is available. Except if a clever unconstrained change in an individual caused the disease, many problems have areas of strength for a set of experiences. A heterozygous individual has a half gamble of giving the disease to their descendants. People with autosomal dominant diseases have a wide range of illness severity, and those with a dominant feature may even not have any symptoms (Pedersen *et al.,* 2003). Hereditary material is coordinated into DNA-protein buildings called chromosomes inside the core. Females have two X chromosomes, though men have one X and one Y chromosome. X-connected alludes to an infection that is welcomed on by a flawed quality tracked down on the X chromosome. All male kids that acquire an X-connected change are impacted because the Y chromosome of the XY pair misses the mark on remunerating typical quality. Since the change is on the X chromosome and guys just give the Y chromosome to their children during preparation, fathers don't give the sickness to their children. However, they can pass on the carrier condition to their daughters, which is a defective X chromosome. A heterozygous female transporter, then again, has a half possibility of bringing forth a transporter little female or male child who is impacted (Ridker *et al.,* 2003). X-connected legacy is