# BIOACTIVE COMPOUNDS FROM PLANT ORIGIN

Extraction, Applications, and Potential Health Benefits

*Innovations in Plant Science for Better Health: From Soil to Fork*

# BIOACTIVE COMPOUNDS FROM PLANT ORIGIN

## Extraction, Applications, and Potential Health Benefits

*Edited by*

**Hafiz Ansar Rasul Suleria, PhD**

**Colin Barrow, PhD**

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**Dr. Hafiz Ansar Rasul Suleria**
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The objective of this new book series is to offer academia, engineers, technologists, and users from different disciplines information to gain knowledge on the breadth and depth of this multifaceted field. The volumes will explore the fields of phytochemistry, along with its potential and extraction techniques. The volumes will discuss the therapeutic perspectives of biochemical compounds in plants and animal and marine sources in an interdisciplinary manner because the field requires knowledge of many areas, including agricultural, food, and chemical engineering; manufacturing technology along with applications from diverse fields like chemistry; herbal drug technology; microbiology; animal husbandry; and food science; etc. There is an urgent need to explore and investigate the innovations, current shortcomings, and future challenges in this growing area of research.

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Dr. Hafiz Suleria is an eminent young researcher in the field of food science and nutrition. Currently, he is an Honorary Fellow at the Diamantina Institute, Faculty of Medicine, The University of Queensland (UQ), Australia. Before joining the UQ, he worked as a lecturer in the Department of Food Sciences, Government College University Faisalabad, Pakistan. He also worked as a Research Associate in a PAK-US Joint Project funded by the Higher Education Commission, Pakistan, and Department of State, USA, with the collaboration of the University of Massachusetts, USA, and the National Institute of Food Science and Technology, University of Agriculture, Faisalabad, Pakistan.

Dr. Suleria's major research focus is on food science and nutrition, particularly in screening of bioactive molecules from different plant, marine, and animal sources, using various cutting-edge techniques, such as isolation, purification, and characterization. He also did research work on functional foods, nutraceuticals, and alternative medicine. He has published more than 60 peer-reviewed scientific papers in different reputed/impacted journals. He is also in collaboration with more than five universities where he is working as a co-supervisor/special member for PhD and postgraduate students and also involved in joint publications, projects, and grants.

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# ABOUT THE EDITOR

**Hafiz Ansar Rasul Suleria, PhD**, is the Alfred Deakin Research Fellow at Deakin University, Geelong, Victoria, Australia. Recently, he has completed a postdoctoral fellowship at the Department of Food, Nutrition, Dietetic and Health at Kansas State University, Manhattan, Kansas, USA. He is an Honorary Fellow in the Diamantina Institute, Faculty of Medicine, The University of Queensland, Australia. Dr. Suleria has been awarded an International Postgraduate Research Scholarship (IPRS) and an Australian Postgraduate Award (APA) for his PhD research at the University of Queensland (UQ) School of Medicine, the Translational Research Institute (TRI), in collaboration with the Commonwealth and Scientific and Industrial Research Organization (CSIRO, Australia).

Before joining the UQ, he worked as a Lecturer in the Department of Food Sciences at the Government College University, Faisalabad, Pakistan. He also worked as a Research Associate in the PAK-US Joint Project funded by the Higher Education Commission, Pakistan, and the Department of State, USA, with the collaboration of the University of Massachusetts, USA, and the National Institute of Food Science and Technology, University of Agriculture, Faisalabad, Pakistan.

His major research focus is on food nutrition, particularly in the screening of bioactive molecules—isolation, purification, and characterization using various cutting-edge techniques from different plants, marine, and animal sources, *in vitro*, *in vivo* bioactivities, cell culture and animal modeling. He has worked on functional foods and nutraceuticals, food and function, and alternative medicine.

Dr. Suleria has published more than 60 peer-reviewed scientific papers in different reputed/impact journals. He is also in collaboration with more than ten universities where he is working as a co-supervisor/special member for PhD and postgraduate students and also involved in joint publications, projects, and grants.

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# ABOUT CO-EDITOR

**Colin Barrow, PhD**, is the Alfred Deakin Professor and Chair of Biotechnology at Deakin University, Geelong, Victoria, Australia, where he is Director of the Centre for Chemistry and Biotechnology. He has previously published two books, including one entitled *Marine Nutraceuticals and Functional Foods*. Dr. Barrow has an H-index of 43, with more than 300 peer-reviewed publications and over 8000 total citations.

Dr. Barrow has held senior roles in both industry and academia. Prior to joining Deakin University, he spent eight years leading the research and development at Ocean Nutrition Canada (ONC) as Executive Vice President of Research and Development. ONC was the world leader in research and commercialization of large scale omega-3 processing and functional food ingredient development and the largest marine biotechnology company in Canada.

He was previously on the Expert Advisory Committee for the Canadian Natural Health Product Directorate (NHPD), is a founding member of the International Society for Nutraceuticals and Functional Foods (ISNFF), and was a member of Board of Directors for the International Society for the Study of Fatty Acids and Lipids (ISSFAL). Professor Barrow was awarded the Nova Scotia Biotechnology and Life Sciences Industry Association (BIONOVA) award for Research Excellence in 2007. He was appointed Guest Professor at Yunnan Minzu University (2015 to 2018), at Qingdao University (2014 onwards), and at the Oil Crops Research Institute Chinese Academy of Agricultural Sciences (2017 to 2022).

His research focuses on food biotechnology and the application of nanomaterials and enzymes for industrial purposes, including structure-function of lipases and graphene for biological applications, as well as a broad spectrum of natural products chemistry, biological chemistry, and food chemistry. Professor Barrow has a PhD in chemistry from the University of Canterbury in New Zealand and an MBA from Penn State University in the USA.

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# ABBREVIATIONS

| | |
|---|---|
| 3,4-DHS | 3,4-dihydroxy-trans-stilbene |
| 4,40-DHS | 4-hydroxy-trans-stilbene |
| ABA | abscisic acid |
| ABTS | 2,2-azinobis-3-ethylbinzothiazoline-6-sulfonic acid |
| ACE | angiotensin converting enzyme |
| ACF | aberrant crypt foci |
| AChE | acetylcholinesterase |
| ACR | acrylamide |
| ADP | adenosine diphosphosphate |
| AGE | aged garlic extract |
| AGPs | antibiotic growth promoters |
| AIDS | acquired immune deficiency syndrome |
| ALA | alpha lipoic acid |
| ALT | alanine aminotransferase |
| AMK | AMP-activated protein kinase |
| AMP | adenosine monophosphate |
| AMR | antimicrobial resistance |
| APC | allophycocyanin |
| AST | aspartate aminotransferase |
| ATP | adenosine triphosphate |
| B-PE | B-phycoerythrin |
| BCBD | β-carotene bleaching test |
| BDNF | brain-derived neurotrophic factor |
| BHA | butylated hydroxyl anisole |
| BHT | butylated hydroxyl toluene |
| BOD | biodegradable |
| cAMP | cyclic adenosine monophosphate |
| CAT | catalase |
| CCl4 | carbon tetrachloride |
| CD4 | cluster of differentiation-4 |
| CHD | coronary heart diseases |
| CI | confidence interval |
| CNS | central nervous system |

| | |
|---|---|
| COX-2 | cyclooxygenase-2 |
| CP | cyclophosphamide |
| CSE | conventional solvent extraction |
| CVD | cardiovascular disease |
| DADS | diallyl disulfide |
| DAS | diallyl sulfide |
| DATS | diallyl trisulfide |
| DEAE | diethylaminoethyl |
| DHA | docosahexaenoic acid |
| DMH | 1,2-dimethylhydrazine |
| DMPD | N-N dimethyl-P-phenylenediamine |
| DNA | deoxyribonucleic acid |
| DPPH | 1,1-diphenyl-2-picrylhydrazyl |
| DSSC | dye-sensitized solar cell |
| DW | dry weight |
| E102 | tartrazine |
| E110 | sunset yellow FCF |
| E127 | erythrosine |
| E129 | allura red |
| EAAE | enzyme-assisted aqueous extraction |
| EACC | Ehrlich ascites carcinoma cell |
| EACP | enzyme-assisted cold pressing |
| EAE | enzyme-assisted extraction |
| ECM | extracellular matrix |
| EDR | endothelium-dependent relaxation |
| EE | ether extract |
| EFSA | European Food Safety Authority |
| eNOS | endothelial nitric oxide synthase |
| EPA | eicosapentaenoic acid |
| EPA | Environmental Protection Agency |
| ER | endoplasmic reticulum |
| ERK | extracellular signal-regulated kinases |
| ESVAC | European Surveillance of Veterinary Antimicrobial Consumption |
| EU | European Union |
| FAS | fatty acid synthase enzyme |
| FCAT | Freund's complete adjuvant test |
| FDA | Food and Drug Administration |

| | |
|---|---|
| FRAP | ferric reducing antioxidant power |
| GABA | gamma-aminobutyric acid |
| GADD | growth arrest and DNA damage |
| GC-MS | gas chromatography mass spectrometry |
| GIT | gastro intestinal tract |
| GLUT | glucose transporter |
| GPx | glutathione peroxidase |
| GR | glutathione reductase |
| GRAS | generally recognized as safe |
| GRP | glucose-regulated protein |
| GRx | glutathion reductase |
| GSH | glutathione |
| GSH-Px | glutathione peroxidase |
| GSP | grape seeds proanthocyanidins |
| H1703 | lung squamous cell carcinoma |
| HCC | hepatocellular carcinoma |
| HCT116 | human colon cancer cell |
| HDFa | human dermal fibroblasts adult |
| HDL | high-density lipoproteins |
| HepG2 | human hepatocarcinoma cell |
| HFD | high fructose diet |
| HHP | high hydrostatic pressure |
| HHPE | high hydrostatic pressure extraction |
| HIF-1α | hypoxia inducible factor-1α |
| HIV | human immunodeficiency virus |
| HMGCR | 3-hydroxy-3-methylglutaryl-coenzyme A reductase |
| HO-1 | heme oxygenasse-1 |
| HPLC | high-performance liquid chromatography |
| HRS | hydroxyl radical scavenging |
| HSV-1 | herpes simplex virus-1 |
| Iκβ | inhibitor of κβ |
| IC50 | inhibitory concentration 50 |
| IDDM | insulin-dependent diabetes mellitus |
| IDF | International Diabetes Federation |
| IL | interleukin |
| IL-1β | interleukin-1 beta |
| IL-6 | interleukin-6 |
| IPC | International Poultry Council |

| | |
|---|---|
| IVD | intervertebral disc |
| JNK | c-Jun N-terminal kinases |
| K562 | human chronic myeloid leukemia cell |
| KK-Ay | type 2 diabetic model |
| LDH | lactate dehydrogenase |
| LDL | low-density lipoproteins |
| LLE | liquid–liquid extraction |
| LLL | combination of linoleic, linoleic, and linoleic |
| LO | lipooxygenase activity |
| LPS | lipopolysaccharide |
| MAE | microwave-assisted extraction |
| MAP | microwave-assisted processing |
| MAPK | mitogen-activated protein kinase |
| MCF-7 | human mammary cancer cell |
| MDA | malondialdehyde |
| MDA-MB-231 | breast tumor cell lines from pleural effusions |
| MDM-LDL | malondialdehyde-modified-LDL |
| MDR-1 | multidrug resistant protein-1 |
| MEP | mevalonic acid pathway |
| MF | mounting frame |
| MFRM | mango fruit reject meal |
| MHG | microwave hydrodiffusion and gravity |
| MIC | minimum inhibitory concentration |
| MMC | mitomycin C |
| MMP | mitochondrial membrane potential |
| MMP 9 | matrix metalloproteinase 9 |
| mRNA | messenger ribonucleic acid |
| mTOR | mammalian target of rapamycin |
| NF-κB | nuclear factor kappa-light-chain-enhancer of activated B cells |
| NIDDM | non-insulin-dependent diabetes mellitus |
| NMDA | m-methyl-D-aspartate |
| NMR | nuclear magnetic resonance |
| NO | nitric oxide |
| NOS | nitric oxide synthase |
| NPQ | non-photosynthetic quenching |
| NQO-1 | NADPH: quinone oxidoreductase 1 |
| NSCLC | nonsmall cell lung cancer cell |

| | |
|---|---|
| NSS | neurological severity score |
| ODC | ornithine decarboxylase |
| OH | ohmic heating |
| OLL | combination of oleic, linoleic, and linoleic |
| ORAC | oxygen radical absorbance capacity |
| ORCs | olfactory receptor cells |
| OVA | ovalbumin |
| p-38 | mitogen-activated protein kinases |
| PABC | pro-oxidant–antioxidant balance |
| PAL | phenylalanine ammonialyase |
| PEF | pulsed electric field |
| Phospho-AKT | protein kinase B (PKB) or serine/threonine-specific protein kinase |
| PLE | pressurized liquid extraction |
| PLL | combination of palmitic, linoleic, and linoleic |
| POL | combination of palmitic, oleic, and linoleic |
| POP | persistent organic pollutants |
| PP | phenylpropanoid |
| PPARy | peroxisome proliferator-activated receptors |
| PTZ | pentylenetetrazol |
| PUFA | polyunsaturated fatty acids |
| R-PE | R-phycoerythrin |
| RAAS | renin angiotensin aldosterone system |
| RE | retinol equivalents |
| ROS | reactive oxygen species |
| RSV | respiratory syncytial virus |
| SAC | S-allyl cysteine |
| SAMC | S-allylmercaptocysteine |
| SF | supercritical fluids |
| SFA | saturated fatty acids |
| SFE | supercritical fluid extraction |
| SI | Stimulation Index |
| SIRT | sirtuin (silent mating-type information regulation 2 homolog) |
| SNPs | silver nanoparticles |
| SOD | superoxide dismutase |
| STZ | streptozotocin |
| TAC | total antioxidant capacity |

| | |
|---|---|
| TAG | triacyl glycerol |
| TBARS | thiobarbituraic acid-reactive species |
| TBI | traumatic brain injury |
| TC | total cholesterol |
| TEAC | trolox equivalent antioxidant capacity |
| TG | triglycerides |
| TGF | tumor growth factor |
| TLR | toll-like receptor |
| TNF | tumor necrosis factor |
| TPC | total phenolic content |
| TrKB | tropomyosin receptor Kinase B |
| TUNEL | terminal deoxynucleotidyl transferase dUTP nick end labeling |
| U937 | human histiocytic lymphoma cell line |
| UAE | ultrasound-assisted extraction |
| UCP | uncoupling protein |
| UFA | unsaturated fatty acids |
| UNESCO | United Nations Educational, Scientific and Cultural Organization |
| UPE | ultrahigh pressure extraction |
| USDA | United States Department of Agriculture |
| UV | ultraviolet |
| UVB | ultraviolet B |
| VDC | voltage-dependent $Ca^{2+}$ channel |
| VLDL | very low-density lipoproteins |
| WAT | white adipose tissues |
| WHO | World Health Organization |
| XO | xanthine oxidase |

# PREFACE

We introduce this book volume under the book series Innovations in Plant Science for Better Health: From Soil to Fork, published by Apple Academic Press. This book mainly covers the current scenario of the research and case studies and the importance of phytochemicals in therapeutics, under two main parts: Part I: Extraction of Bioactive Compounds and Their Applications, and Part II: Bioactive Compounds and Health Claims.

Part I describes the advances in the extraction of bioactive compounds from various sources. Advanced extraction techniques such as enzyme-assisted, microwave-assisted, ultrasound-assisted, pressurized liquid extraction and supercritical extraction techniques are described in detail. Natural products and their bioactive compounds are being increasingly utilized in preventive and therapeutic medication. Bioactive compounds have been utilized for the production of pharmaceutical supplements and more recently as food additives to increase the functionality of foods.

Part II covers the role of different bioactive compounds and their health-promoting potential for lifestyle diseases. The incorporation of any functional foods, nutraceuticals, and bioactives in the daily diet is a beneficial endeavor to help prevent the progression of chronic disorders. This section explains the botany, physical characteristics, uniqueness, uses, distribution, importance, phytochemistry, traditional importance, nutritional importance, bioactivities, and future trends of different functional foods. Functional foods, beyond providing basic nutrition, may offer a potentially positive effect on health and cure various disease conditions such as metabolic disorders, cancer, and chronic inflammatory reactions.

This book volume sheds light on the potential of plants for human health from different technological aspects and contributes to the ocean of knowledge on food science and nutrition. We hope that this compendium will be useful for students and researchers of academia as well as for persons working with the food, nutraceuticals, and herbal industries.

The contributions by the cooperating authors to this book volume have been most valuable in the compilation. Their names are mentioned in each chapter and in the list of contributors. We appreciate you all for having

patience with our editorial skills. This book would not have been written without the valuable cooperation of these investigators—many of whom are renowned scientists—who have worked in the field of food science, biochemistry, and nutrition throughout their professional careers. I am glad to introduce my mentor and a coeditor, Prof. Colin Barrow, who brings his expertise and innovative ideas on bioactive compound, drug discovery, and separation sciences in this book.

The goal of this book volume is to guide the world science community on how bioactive compounds can alleviate us from various conditions and diseases.

We will like to thank editorial and production staff, and Ashish Kumar, Publisher and President at Apple Academic Press, Inc., for making every effort to publish this book when all are concerned with health issues.

We request that readers offer us constructive suggestions that may help to improve future works.

I thank Dr. Megh R. Goyal for his leadership and for inviting me to join his team. He is a world-renowned scientist and engineer with expertise in agricultural and biological engineering. Truly he is giver and a model for budding scientists. I am on board to learn.

**— Hafiz Suleria**

# PART I

# Extraction of Bioactive Compounds and Their Applications

## CHAPTER 1

# EXTRACTION OF BIOACTIVE MOLECULES: CONVENTIONAL VERSUS NOVEL METHODS

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### ABSTRACT

Bioactive compounds are widely distributed in plant sources and are the most abundant secondary metabolites of the plants. Based on chemical characterization, they include: glycosides, flavonoids, tannins, terpenoids, lignans, alkaloids, peptides, and others. The extraction of bioactive molecules has drawn increasing attention due to their antioxidant and therapeutic potential through their interactions with vascular endothelial cells to prevent cardiovascular disorders and cancer. Although the development in chromatographic and spectrometric analytical techniques has significant contribution in the detection of bioactive components, the success depends on the method of extraction as two-third part of analytical work is required to get these components. In conventional extraction methods, several combinations of temperature, solvent, agitation speed, and extraction time have been optimized to get maximum yields, but these conventional proposals are creating burden on environment due to high temperatures for a long time and secondly, affect the

heat-sensitive bioactive components. Alternatively, application of novel techniques like ultrasound, microwave, high pressure, pulsed electric field, supercritical fluid, and others is more welcoming due to less environmental burden in the form of lessened usage of organic solvents, low working temperatures, short duration, and improved quality and yield with high selectivity to compounds of interest. The efficiencies of both either conventional or novel extraction methods are typically based on the input parameters, complexity of plant source, structural conformation of bioactive components, and skill to up-scale them. This chapter aims to discuss basic mechanisms involved in the extraction of bioactive molecules from plant material through conventional as well as novel extraction techniques.

## 1.1 INTRODUCTION

Bioactive compounds are secondary metabolites in plants that are prompting toxicological and pharmacological effects in both animals and man. The production of these secondary metabolites within the plants took place as a result of primary metabolic and biosynthetic pathways for compounds related with growth and development of the plant, therefore, they are considered as by-products of plant cells metabolism.[7] These bioactive compounds are well known due to their significant functionality in plants, for instance, (1) during photosynthesis, flavonoids act as free radicals scavengers, (2) terpenoids can appeal pollinators or seed dispersers, (3) alkaloids repels insects or herbivore animals, and (4) likewise, other secondary metabolites indulge in many different functions within the plants.[90]

Majority of the plants produce bioactive compounds including food and feed plants, but the higher concentration of bioactive molecules are present in medicinal or poisonous plants.[83,98] Various studies confirm that these secondary compounds have a protective action on human health and are the key elements of a healthy and balanced diet.[20,143] They have beneficial effect on prevention of cardiovascular diseases, inflammation, glucose intolerance, and obesity.[12,162] According to World Health Organization, the approximate share of world's population that relies on their primary health care from plant-derived natural medicines is 65–80%.[158,48] For instance, flavonoid is most important phytochemical capable

of controlling the incidence of diabetes, cancer, and cardiovascular diseases.[71] Catechin, another bioactive molecule present in green tea, is effective against obesity.[91] Bioactive compounds also possess antioxidant activity which decreases the deleterious effects of substances with high oxidative potential. This antioxidant property is principally designated to their redox potential which lets them to work as reducing agents.[83] Thus being an important constituent of human diet, the extraction of biochemical molecules from natural plant sources is of keen interest for the researchers.

## 1.2 CATEGORIES OF BIOACTIVE MOLECULES

Classification of plants bioactive molecules depends on different criteria. They could be presented clinically, toxicologically, pharmacologically, or botanically; but it is complicated as even chemically related compounds can possess different clinical outcomes or even less genetically related species could produce dissimilar bioactive molecules.[7] Therefore, it is preferable to classify them according to the chemical classes and biochemical pathways. According to Croteau et al.[37] and Taiz et al.,[141] bioactive molecules from plant sources are categorized into: (1) terpenes and terpenoids (roughly 25,000 compounds) produced by mevalonic acid and non-mevalonate (MEP) pathways, (2) alkaloids (roughly 12,000 compounds) produced through shikimic acid pathway, and (3) phenolic compounds (roughly 8000 compounds) produced by malonic acid and shikimic acid pathways.

### *1.2.1 TERPENES*

Among the natural products, the terpenoids occupied the largest group, also used in number of industrial sectors as fragrances, spices, and flavors also used in cosmetics and perfume-making industries. Huge types of terpenoids have been identified, that is, 25,000; these compounds have major role in defense against biotic and abiotic factors and also act as source of attraction for the insects of pollination.[136] Terpenoids have been studied for their role in medicine and biotechnology. Terpenes are hydrocarbon-based compounds which contain a structure derived from isoprene which

give rise to another structure which may also be divided into isopentane units.[119]

There are two major pathways to produce terpenes, that is, conventional acetate-mevalonic acid and non-mevalonic acid pathways. The conventional acetate-mevalonic acid pathway is operated in the cytosol and mitochondria of plant cells; there, various compounds are synthesized, namely, sterols, sesquiterpenes, and ubiquinones.[85] While the non-mevalonic acid pathway takes place in plastids of plant cells and prepare compounds like hemi-, mono-, sesqui-, and diterpenes, additionally carotenoids and phytol tail of chlorophyll.[22]

Odors and flavors of terpenoids are strong. These compounds have wide range of their action which is being used for herbal remedies. Among these variations, particular examples are antibacterial, antineoplastic, antiviral effects along with metabolic stimulation which are very important. Toxicity of these compounds is associated with their concentrated form as volatile oils. Terpenoids mainly belongs to family *Lamiaceae* (thyme family) but may be present in other similar families.[7,15]

In fragrance and perfume industries, monoterpenoids are major constituent of various essential oils while other acyclic compounds are geraniol, linalool, and myrcene. Camphor, menthol, limonene, and pinene are cyclic structures. Due to higher boiling point, diterpenes do not possess the characteristics of essential oils and are considered as component of plant resins.[50] Terpenoids including squiterpenes, compounds with three isoprene units are mostly present in aliphatic bi- and tricyclic forms. Farnesol, a aliphatic bicyclic form, is an important intermediate in terpenoid synthesis. Arteether, extracted from *Artemisia annua*, is a sesquiterpene lactone derived from artemisinin and nowadays, used as an antimalarial drug. Triterpenes (C30) are mainly composed of six isoprene structures and are formed from squalene during biosynthesis. Such compounds have higher melting points, are colorless, occur in solid form, and mainly found in resins, cork, and cutin. Steroids, saponins, and cardiac glycosides are produced from triterpenoids which are pharmacologically active. From seeds of *Azadirachta indica* a powerful insect ant-feedent is produced. Among other tri-terpenoids, cucurbitacins and limonins are effective insect steroid hormone antagonists.[102]

Plant steroids which are hydroxylated at C3 position are classified as sterols. Steroids are altered forms of triterpenes and in animals act as necessary hormones, for example, estrogens such as progesterone and

androgens such as testosterone, coenzymes, and provitamins. Diosgenin is the important source of much progesterone which is derived semisynthetically. On the other hand, amaryllidaceae, dioscoreaceae and liliaceae, and dicot families (Solanaceace and Scrophulariaceace. Saponins) are important source of saponins (C27). These compounds are composed of mainly two parts, namely, aglycone (genin or triterpene) and glycone (sugar). Important preparations based upon saponins are licorice (*Glycerrhiza glabra*), primula root (*Primula*), sarsaparilla root (*Sarsaparilla*), ginseng (*Panax ginseng*) and ivy leaves (*Hedera*). Glycyrrhizins are the salt form of ammonium and calcium with glycyrrhizic acid, and on sucrose scale, they are 50–100 times sweeter.[152]

### *1.2.2 ALKALOIDS*

The alkaloids have potent activity and bitter taste. They are heterocyclic compounds containing nitrogen. In more than 150 families, 12,000 types of these compounds are present in plants. *Papaveraceae, Apocynaceae, Ranunculaceae, Fabaceae, Rubiaceae, Solanaceae*, and *Rutaceae* are important families of alkaloids, while less common lower plants and fungi (ergot alkaloids) also contain these compounds.[77] Alkaloids are present in isomeric forms as salts of organic acids like malic, oxalic, lactic, citric, tannic, tartaric, and other acids in plants. On the other hand, few weak basic alkaloids (such as nicotine) present freely in plant systems. Some members of alkaloids are also found in glycosidic form with galactose, glucose, and rhamnose such as solanine. They also occur in the form of amides (piperine), and as esters (cocaine and atropine) of organic acids.[82,101]

Plants contain alkaloids in their various parts such as large amounts of these compounds are present in seeds (nux vomica, *Areca*), stem bark (cinchona and pomegranate), and roots (aconite and belladonna). Alkaloids are abundant in dicots as compared to monocots.[126] Alkaloids are used as narcotics, stimulants, poisons, and pharmaceuticals due to their potent activity. Some of the most common examples of alkaloids which are being used are the anticancer agent—vinblastine, the muscle relaxant—(+)tubocurarine, analgesics—codeine and morphine, the antiarrhythmic agent—ajmalicine, the gout suppressant—colchicine, the sedative—scopolamine, and the antibiotic—sanguinarine. Caffeine in coffee and tea along with

nicotine in all preparations such as chewing, smoking, etc. are extensively used on daily basis.[100]

Different clinical properties are found in different alkaloid groups. For instance, tropane alkaloids are abundantly found in *Solanaceae* family, for example, in *Atropa belladonna, Datura* spp., and *Hyoscyamus niger*. The compounds of these alkaloid groups contain anticholinergic effect to lessen the smooth muscle spasms, pain, and hypersecretion; therefore, these compounds are extremely medicinally important. *Asteraceae* (daisy family), particularly *Boraginaceae* (borage family) and *Senecio* spp. (Ragworts) are the good source of pyrrolizidine alkaloids. After bioactivation, they exert adverse effects on human health. Isoquinoline alkaloids are present in *Berberidaceae* (barberry family) and *Papaveraceae* (poppy family). Such compounds have wide range of biochemical effects in humans by controlling different malady conditions (cancer cells, bacteria, and pain) along with improvement in bone marrow leucocytes and myocardial contractility.[109] *Coffea arabica* (coffee) and *Theobroma cacao* (cacao) are the main sources of methylxanthine alkaloids which show an important impact on neurological systems of humans and animals. Similarly another group of alkaloids, pseudoalkaloids, which are chemically close to alkaloid, affect the central nervous system. These compounds are synthesized by species in *Apiaceae* (carrot family), for example, *Cicuta virosa* (cowbane) and *Conium maculatum* (hemlock).

### 1.2.3 POLYPHENOLS

Polyphenols are widely distributed in nature. They are the secondary compounds of plant kingdom. Almost 8000 types of phenolic compounds are identified and classified into various subgroups based on the number of phenol rings present and the structural elements which bind such rings to one another. These classes include phenolic acids (hydroxycinnamic acids and hydroxybenzoic acids), flavonoids (flavonols, flavanols, flavanones, flavones, proanthocyanidins, and isoflavones), tannins, stilbenes, and lignans. These classes of polyphenols are present in plants and in various foods of plant origin.[98,99] Simple phenolic compounds have at least one OH-group bounded to an aromatic ring, such as catechol while majority of compounds contain C6C1 carbon skeleton having carbonyl group bounded to the aromatic ring.[60] Mostly, phenolic compounds are prepared through shikimate pathway, but sometimes a few phenolic

compounds, for example, orcinols and quinones, are synthesized by the polyketide pathway. Phenolics synthesized from either pathway shared common structure such as flavonoids, stilbenes, pyrones, and xanthones.[91] Majority of phenolic compounds are present in leaves, woody parts of plants such as barks, stems, flowering tissues, etc.[74] Phenolics add taste, color, and nutritional properties to the fruit.[30]

Flavonoids compounds are composed of two phenolic rings joined through a pyranring and proanthocyanidins, the polymers of flavonoid units both of which occurred in glycosidic forms. Any compound containing phenol group acts as an antioxidant. Other actions include reducing inflammation and carcinogenicity. Isoflavones are also known as phytoestrogens. A long range of pigments is present in plants, for example, flavonoids and proanthocyanidins. *Fabaeceae* (bean family) are the main source of the isoflavones.[36]

Tannins exist in two types: condensed and hydrolyzable, depending on their structural complexity. Condensed tannins are large oligomers of flavonoid units, whereas hydrolyzable tannins are composed of glycosidic center (commonly glucose) with several catechin/phenolic acid derivatives. Solubility of tannins decreased with the increase in size of the molecule. Tannins could be antinutritional as they can bind with proteins and minerals while bigger tannins are served as astringents in various diseases (diarrhea, transudate, and skin bleeding). These compounds are present in wide range in plant kingdom. *Fagaceae* (beech family) and *Polygonaceae* (knotweed family) are few examples of plants containing tannins.[14]

Lignans contain different functional groups and consist of two phenylpropanoid units to form an 18-carbon skeleton. These compounds are present within the cell membrane and perform specification functions as they contain lipophilic properties.[52] Lignans are present in different concentrations in different plant species but higher amounts are discovered in oilseeds. Phytoestrogenic, cathartic, or antineoplastic effects are associated with lignans.[65]

## 1.2.4 OTHER BIOACTIVE COMPOUNDS

### 1.2.4.1 PROTEINS AND PEPTIDES

Proteins perform an extremely important role in food and feed. Proteins components are absorbed into the blood from intestinal tissues and provide

building blocks of the body protein. Besides these, many proteins also act as bioactive molecules.[108] These bioactive proteins are unable to hydrolyzed in GIT, rather than absorbed in blood and exert their particular function in the body. Such proteins are produced by *Euphorbiaceae* (spurge family) and *Ricinus communis* (castor bean). For example, ricin tends to prevent the synthesis of proteins and produce gradual effects in animals and humans. These proteins exist in minor quantity in seeds of several species of *Fabaceae* (bean family). Symptoms related to colic and other metabolic disorders may produce if seeds are not heat treated to inactivate lectin.[79]

### *1.2.4.2 GLYCOSIDES*

Glycosides may originate from various types of secondary metabolites which are bound with a monosaccharide, oligo-saccharide, or uronic acid. Therefore, it contains two groups, first one is glycine (saccharide or uronic acid part) while remaining part is known as aglycon. Cyanogenic glycosides, cardiac glycosides, anthraquinone glycosides, saponins, and glucosinolates are the some main groups of glycosides. Flavonoids are also found as glycosides. After intake of glycosides, it hydrolyzes in the colonic part, while the more hydrophobic glycosides (aglycone) might be absorbed.[160]

Steroidal structure is present in aglycones of cardiac glycosides. They inhibit the $Na^+/K^+$-ATPase-pumps operated in the cell membranes. Aglycones of cyanogenic glycosides are derived from the amino acids.[112] Hypothyroidism may result as these compounds may interfere with utilization of iodine. Sulfur containing amino acids are present in amino acid-derived aglycones which have pungent smell. In various cells, these compounds exert a complex effect on cytochrome (P450 isoforms) and therefore it decreases the hepatic bioactivation of environmental procarcinogens. Majority of saponins (soap-forming compound) are present as glycosides. Emulsifying properties are associated with saponin glycosides which are comparatively big molecules having hydrophilic and hydrophobic aglycone parts.

## 1.3 IMPORTANCE OF EXTRACTION

Extraction is the primary stage in medicinal plant research with the significant impact on the final outcome. Bioactive compounds contain the pool of molecules having broad diversity of functionalities and structures that present an important role in the production of food additives, functional foods, and nutraceuticals. The distribution of bioactive compounds in nature vary according to their concentration, some of them are present at low level, whereas some compounds, such as polyphenols, can be found in higher concentration. Therefore, to obtain these compound in adequate level, huge harvesting is required which is quite complicated and unbeneficial related to cost.[72] Although the development in chromatographic and spectrometric analytical techniques has significant contribution in the detection of bioactive components, still success depends on the method of extraction as two-third part of analytical work is required to get these components.[11] The innate obstacles in producing and screening required bioactive compounds have led to the advancement of the novel extraction technologies.

Currently, many researchers and industrialists are involve in finding out various methods to explore the potential of bioactive compounds from natural sources for the prevention and treatment of various human diseases and to meet other needs. The efficiency of these compounds to interact with different biological molecules including DNA and proteins for the production of preferred outcome allows them to be fully utilized in designing therapeutic agents derived from natural products.[6] Hence for this purpose, the extraction of bioactive molecules from plant sources along with the estimation of their quantitative and qualitative properties is important for exploration of new biomolecules to be used by agrochemical and pharmaceutical industry.[68] According to UNESCO in most developing countries, 80% of the world's population relies on the use of herbal products on regular basis to keep good health.[27] The thousands of chemical compounds present in these plants are used for different infectious diseases. These phytochemicals possess beneficial biological activity such as antioxidant, antimicrobial, anticancer, analgesic, antidiarrheal, and wound healing..[45]

Nowadays, the food industry is focusing to manufacture and develop different functional food products. The growing interest of consumer for healthy food makes this new class of food product successful in the market. In general, these functional foods include various different types

and proportions of bioactive compounds.[15] Therefore, functional food can be defined as a new product in which bioactive compounds from different natural sources are incorporated to formulate food with a specific function.[41]

Plaza et al.[118] discuss three main factors to be fulfilled by a functional food. First of all, the effect of functional food should be different as compared to normal diet. Second, there should not be any side effect of developed functional product, and third, it should be beneficial in reducing risk of developing pathological condition and should also help to improve physiological function. Therefore, the desired biomolecules that possess biological activity such as antiviral, antioxidant, antihypertensive, antidiabetic, and so on are extracted from plant sources to be used in formulating different functional products as not all bioactive compounds cover all these aspects.[118] These functional foods help in decrease in cholesterol levels, maintaining remission of Crohn's disease, alleviation of lactose intolerance, inhibition of cancer cell proliferation in vitro and in vivo, and faster relief from diarrhea.[101,62,111] The functional foods that are presently accessible in the market are bakery products, drinks, meat products, cereals, eggs, and spreads.[137] Among all these products, beverages are the most convenient because of their comparative easy handling, processing, and formulation with more complex processed foods.[41,62]

The conventional techniques for the extraction of bioactive compounds used frequently are liquid–liquid or solid–liquid extraction, Soxhlet extraction, maceration, and hydrodistillation, and the advanced methods include subcritical and supercritical extractions, pressurized liquid extraction, ultrasound- and microwave-assisted extractions (MAEs), pulsed electric field extraction, and ohmic extraction. The novel extraction methods are basically used to enhance the release of compounds from the plant matrix. Therefore in the next few years, these technologies could provide an eco-novel approach to boost the production of particular compounds for use as constituents in the manufacturing of functional foods or as nutraceuticals.

## 1.4 CONVENTIONAL EXTRACTION TECHNIQUES

Plant extraction is a pragmatic exercise in light of the fact that distinctive solvents are used at different conditions, for example, temperature and time of extraction.[68] The time, temperature, solvent, pressure, and the

matrix properties of plant part are the most well-known variables influencing extraction methods.[63] The extracting methods, utilized to separate bioactive mixes from plant sources, mostly depend on extracting power of various solvents being used and also on the use of heat and mixing. The most common conventional techniques in order to extract bioactive compounds are Soxhlet extraction, liquid–liquid extraction, evaporation, maceration, and hydrodistillation. In conventional extraction methods, several combinations of temperature, solvent, agitation speed, and extraction time have been optimized to get maximum yields, but these conventional proposals are creating burden on environment due to high temperatures for a long time and also affect the heat-sensitive bioactive components. Some bioactive compounds extracted through these conventional techniques are given in Table 1.1.

### *1.4.1 SOXHLET EXTRACTION*

Soxhlet extraction is a most commonly used conventional technique to extract different compounds from the plant materials. It is an ordinary case of a comprehensive solid–fluid extraction. This procedure relies on the exchange of the target compound(s) from the sample (solid) to appropriate organic solvent(s). It is guaranteed that the extraction solvent (fluid) remains reliably in contact with the sample during this thermal extraction process.[25]

It was specifically designed to extract lipids but currently, it is also used to extract other components from the plant parts. Numerous valuable bioactive compounds were extracted by using the Soxhlet extraction technique from different plant sources.[161] To develop alternative extraction techniques Soxhlet extraction is used as model. Soxhlet extraction technique is effectively used if desired compound has good solubility in solvent and impurities are insoluble in that solvent.[35]

Soxhlet extraction technique is effectively used to extract components from solid sample like sediment, soil, and indoor dust samples. Other semisolid samples including sewage sludge, blood, milk, and fat can also be efficiently used to extracts components by using Soxhlet technique.[42] Soxhlet extraction apparatus consists of a thimble (sample holder), distillation flask, siphon, and condenser as it is evident from Figure 1.1.

Its operation is quite simple; generally, little amount of dry sample is kept in the inner side of the thimble (Fig. 1.1) which is then placed in a distillation flask containing desired solvent. After achieving specific temperature, the solution aspired through siphon. This siphon is used to mix back of the solution in the distillation flask which brings extracted component into the solvent. During operation, desired component remains in distillation flask in the form of solute while solvent moves to the bed of the plant material. This operation is repeated several times until the extraction of desired component is achieved.[56,157] The main advantage of this technique is use of single batch of solvent which is recycled again and

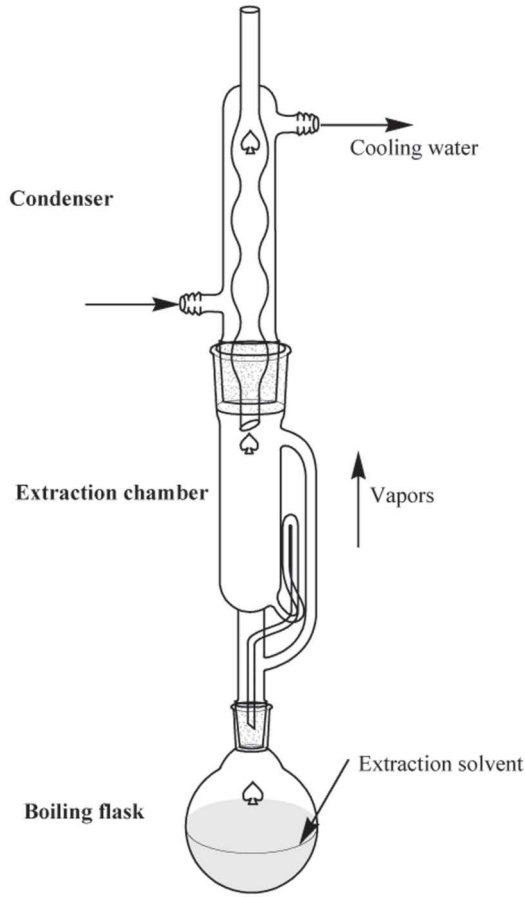


**FIGURE 1.1** Soxhlet extractor.

again during the process. Many disadvantages are also associated with this technique, such as, heat-sensitive compounds cannot be extracted by using Soxhlet apparatus because prolonged heating time may destroy the heat-labile compounds[139] This technique is also not suitable for industrial applications as it have long extraction time and utilizes high amount of hazardous solvents along with other disadvantages.[16]

### *1.4.2 LIQUID–LIQUID EXTRACTION*

For the efficiently extract the bioactive compounds, sample can be pretreated. Liquid–liquid extraction is a useful pre-treatment technique which is most commonly used now a day. It can increase the selectivity by separating analyte from matrix of the sample or by concentrating the desired analyte from high sample volume. This technique also associated with number of disadvantages including the manual working of this mass transfer operation which is laborious and time consuming along with higher demand of chemicals that can adversely affect to the operator, also expensive and cause environmental pollution.[107] Different strategies were used to minimize the risk of abovementioned disadvantages by reducing solution consumption, reduction of operator invention and expose along with increasing the sample rating etc.[31]

A modified liquid–liquid extraction technique, for example, flow-based LLE has been successfully used in different industries like food analysis, pharmaceutical, and clinical, among others which reduces the environmental pollution.[64] A conventional liquid–liquid extraction technique consists of three important components, that is, a phase segmenter, a phase separator, and an extraction coil (Fig. 1.2). Liquid sample is introduced either in a flow process or in a specifically defined volume, into an aqueous stream (which acts as reagent and carrier stream). After introduction of the liquid sample, homogenization process is carried out which results in the formation of reaction zone, directed toward the segmenter part of the liquid–liquid extraction. In this part, the two streams of aqueous and organic immiscible phases remain in contact and a single flow of alternate reproducible zones of both phases is produced. Consequently, in the extraction coil, mass transfer between the two phases multiple interfaces created by the segmentation process is taking place. Finally, in the phase separator, the little–liquid and organic phase parts are continuously

divided into individual streams, one of that contains the analyte directed toward the detector for detection.[23]

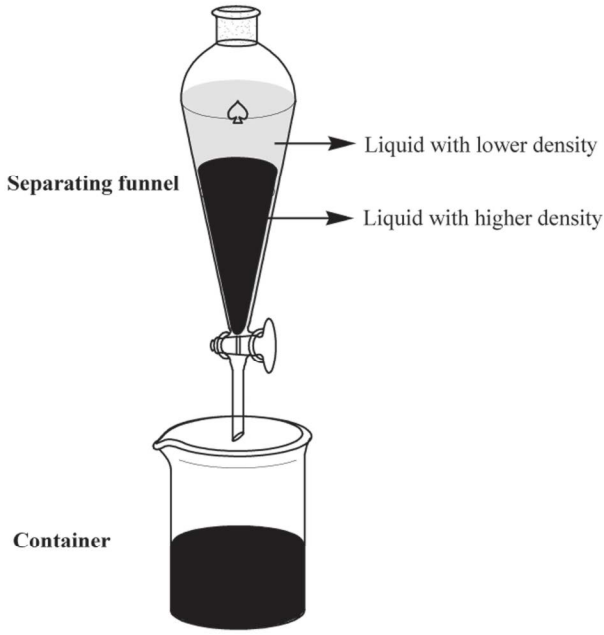


**FIGURE 1.2** Liquid–liquid extractor.

### *1.4.3 MACERATION*

Homemade tonics are prepared by using the maceration technique. It is very famous and inexpensive technique to isolate the oil or other desired components. Its operation is quite simple. Whole sample or coarse powder was kept in the solvent containing stoppered, which remain consistent with solvent for specific time period. During this period, frequent agitation is given until soluble matter dissolved as evident from the Figure 1.3. Heat-sensitive compounds can efficiently extracted by using this technique for example thermolabile drugs.[110] Several steps are associated with maceration process at small scale. Grinding of desired sample is first step which is carried out to increase the surface area. In second step suitable solvent is added. In third step of maceration, the marc which is the solid by-product of this extraction course is forced to recover large quantity of

desired solutions. In forth step, impurities are separated from the obtained strained and the press out liquid by using filtration process. Extraction process help the extraction of bioactive molecules in two ways: (1) by increasing diffusion and (2) by removing concentrated solution from the solid surface for fetching new solvent to get high yield.

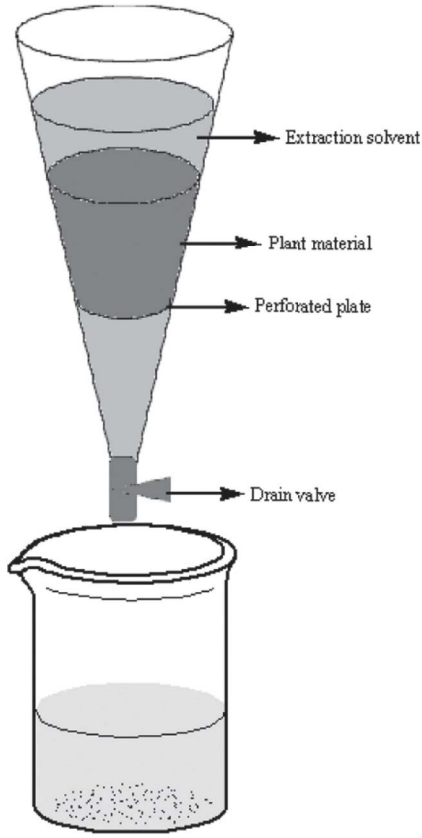


**FIGURE 1.3** Apparatus for maceration.

### *1.4.4 HYDRODISTILLATION*

Hydrodistillation is a conventional technique for extraction of basic oils and bioactive molecules from plants. It does not include organic solvents

in it and usually takes place before plant material gets dehydrated. There are three kinds of known hydrodistillation methods: steam refining, steam and water refining, and direct water refining.[146] In hydrodistillation, to begin with, the plant material is placed in a batch system compartment; second, adequate amount of water is included and then brought to boil.[125] The setup includes condenser and a decanter to gather the condensate and to isolate bioactive molecules from solvent (Fig. 1.4). On the other hand, direct steam is infused into the plant sample. Steam and hot water go about as the principle powerful factors to free bioactive compounds of plant tissue. The vapor mixture of water and oil condenses by indirect cooling of water. The mixture streams from condenser to a container where immiscible part (oil and bioactive mixes) isolates naturally from the water.[135] Three fundamental physicochemical procedures are involved in hydrodistillation: (1) hydrodiffusion, (2) hydrolysis, and (3) disintegration by heat. In this technique, some volatile components may be lost due to high extraction temperature and this drawback restrains its utilization for the extraction of heat-sensitive compounds.

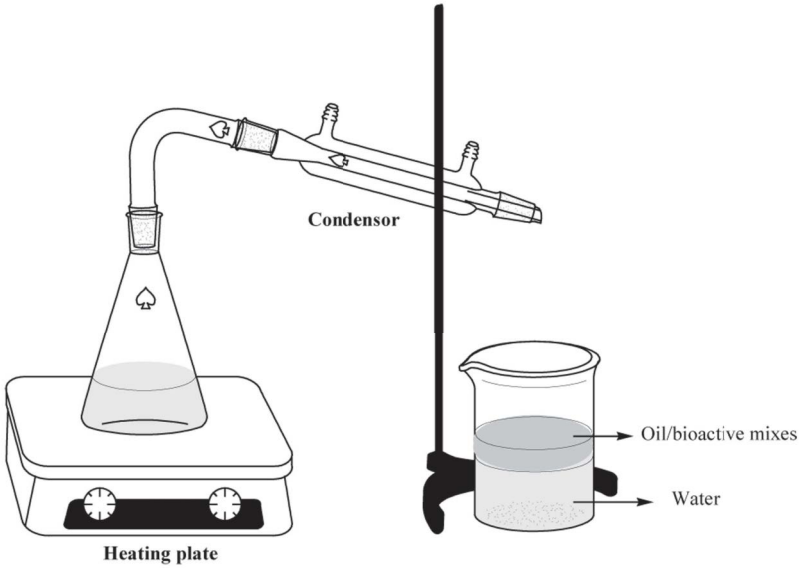


**FIGURE 1.4** Apparatus for hydrodistillation.

**TABLE 1.1** Biomolecules Extraction by Conventional Extraction Methods.

| Conventional method | Bioactive compound | Optimal conditions | Remarks | References |
|---|---|---|---|---|
| **Soxhlet extraction** | Squalene, n- hexadecanoic acid, tetramethyl-2-hexadecen-1-1 and octadecatrienoic acid from agarwood leaves | Solvents: distilled water, hexane, isopropanol and ethanol for 6 h at 60°C | Extraction using hexane as solvent gave highest percentage of oil yield | [87] |
| | Tocopherol, phytol, β-sitosterol, γ-sitosterol from aromatic plant | Solvent: 200 mL of pentane for 4 h at 40°C | Oleoresins were obtained from 10–40 g ground plants | [61] |
| **Liquid–liquid extraction** | Flavanols, kaempferol, quercetin, apigenin, luteolin and myricetin from different vegetables | Solvent: 40 mL 80% methanol, 10 mL 6 M HCl and 80 mg ascorbic acid for 2 h at 90°C | Effective in releasing the aglycone and increasing recovery rate of phenolics from 76.1% to 98.6% | [66] |
| | Polyphenols and carotenoids of blackberry, naranjilla, and tree tomato | Solvent: 60 mL of 70% aqueous acetone containing 2% formic acid, twice for 15 min at 40°C | Major phenolics were extracted in higher amount from fruits | [106] |
| **Maceration** | Phenolic acids and flavonoids of Kinnow peel | Solvent: ethanol, methanol, acetone, and ethyl acetate, macerated for 20 h at 40°C | Extraction with 80% ethanol resulted in the highest yield (18.46%) | [128] |
| | Phenolic compounds and flavonoids from *Eryngium creticum* | Solvent: ethanol, macerated for 48 h with agitation of 360 rpm | About 410.93 mg total yield of bioactive compounds was extracted | [163] |

**TABLE 1.1** *(Continued)*

| Conventional method | Bioactive compound | Optimal conditions | Remarks | References |
|---|---|---|---|---|
| **Hydrodistillation** | Volatile oil of rosemary | Solvent: water for 10 min | Almost 80% oil was extracted including 31.9% 1,8-cineol, 19.7% camphor, 12.8% α-terpineol, 12.2% borneol | [18] |
| | Essential oil from peel of *C. microcarpa* | Solvent: water for 8 h | 94% limonene, β-myrcene (1.8%), linalool (0.4%), and α-terpineol (0.3%) were extracted | [103] |

## 1.5 NOVEL EXTRACTION TECHNIQUES

Conventional extraction has become a least concerned method in food industry due to its various drawbacks like high cost, longer extraction time, thermal decomposition of thermolabile compounds, low extraction selectivity, requirement of high purity solvent, and its evaporation at high amount[56]; therefore, some novel and promising nonconventional extraction techniques are introduced to overcome these limitations. The development of these nonconventional methods came into being during the last 50 years. They acquire less time, give better quality and yield of extract and considered as more environmental friendly due to use of organic and synthetic chemicals in lesser amount. The most frequently used novel methods to extract the bioactive compounds from plant sources are ultrasound,[58,148] ohmic heating,[84] microwave heating,[76] pulsed electric field,[144] extrusion,[97] supercritical fluids,[156,59] and digestion using enzymes.[57] These novel extraction methods include safe solvents auxiliaries, less hazardous chemical synthesis, use of renewable feedstock, design for energy efficiency, lessen derivative formation, design to reduce degradation, and timely analysis for decreased level of pollution and inherently safer chemistry to prevent accident.

These novel nonconventional extraction techniques are further divided into thermal and non- thermal extraction. Thermal extraction methods includes: (1) MAEs and (2) ohmic heating whereas non-thermal extraction has vast methodologies: (1) ultrasound-assisted extraction (UAE), (2) pulse electric field-assisted extraction, (3) supercritical fluid extraction, (4) high-pressure-assisted extraction, and others.

## 1.5.1 THERMAL EXTRACTION METHODS

### 1.5.1.1 MICROWAVE-ASSISTED EXTRACTION

Microwaves have been utilized since World War II following the advancement of radar innovation, and later the main application of microwaves concerned household ovens. The utilization of microwave vitality as a warming source in expository research facilities began in the late 1970s and was applied to corrosive digestions.[2] The improvement of MAEs was first reported by Ganzler et al.[54,53]

The MAE is additionally considered as a novel technique for extricating solvent items into a liquid from an extensive variety of materials utilizing microwave vitality.[115] Microwaves are electromagnetic fields in the frequency range from 300 MHz to 300 GHz. They are composed of two oscillating fields that are opposite, for example, magnetic field and electric field. The principle of microwave heating depends on its immediate effects on polar materials.[89] Electromagnetic vitality is changed over to heat after ionic conduction and dipole rotation mechanism.[70] Heat is produced during ionic conduction mechanism as a result of the resistance of medium to flow ion. Alternatively, ions keep their path along field signs which change repeatedly. This regular change of direction brings about collapse amongst molecules and thus creates heat.

Patil and Shettigar[116] revealed a novel, microwave-assisted solvent extraction advancement known as microwave-assisted processing (MAP). The high-valued compounds are incorporated by microwave-assisted processing from natural sources like phytonutrients, nutraceuticals, and functional foods and from biomass like pharmaceutical actives. There are three successive steps of MAEs which are supposed to be fulfilled for advance extraction as described by Alupului et al.[9]: first, under expanded pressure and temperature, solutes should detached from binding sites of

plant matrix; second, dispersion of solvent crosswise over plant matrix; third, discharge of solutes into solvent from plant matrix. A number of focal points of MAE have been depicted by Cravotto et al.,[34] for example, rapid increase in temperature to get bioactive compounds; increased extract yield, smart equipment size, and decreased thermal gradients. MAE can extricate bioactive compounds more quickly and a superior recuperation is expected than conventional extraction techniques. It is a specific method to remove natural and organometallic compounds that are more integral. MAE is additionally perceived as a green innovation since it lessens the utilization of natural solvent.[9] Very recently, a novel technique called microwave hydrodiffusion and gravity (MHG) has been introduced in the market of extraction by one of the contributor of this book, Prof. Farid Chemat (Fig. 1.5). The efficiency of bioactive extraction of microwave-assisted processing is listed in Table 1.2.

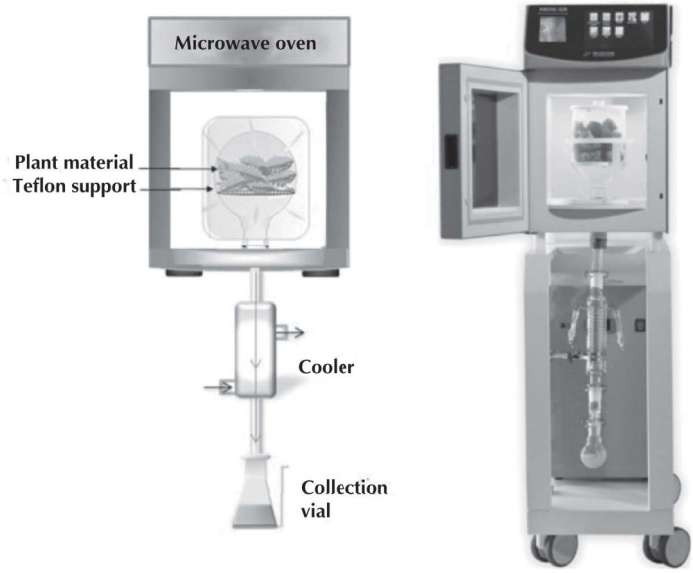


**FIGURE 1.5 (See color insert.)** Microwave hydrodiffusion and gravity (MHG) extraction system.

### *1.5.1.2 OHMIC HEAT-ASSISTED EXTRACTION*

Ohmic heating, also termed as electroconductive heating, uses the innate electrical confrontation of plant material to create heat[153] (Fig. 1.6). Most

plant materials contain ionic components, for example, acids and salts, permitting the conduction of electrical current.[114] This phenomenon can be used to create heat inside the item, changing the electrical vitality into thermal vitality, and hence heating plant materials at outstandingly quick rates without the requirement for a heating medium. This procedure avoids extreme thermal impairment to heat-sensitive constituents, for example, pigments and vitamins.[26,134] They have appeared to be mellow handling advancements protecting sensory, nutritional, structural, and functional properties of items superior to traditional methodologies.[80,151] Specifically, the extraction procedure has been utilized to expand the productivity of solute dispersion all through the membrane (electro-osmosis impact), bringing about a superior quality product.[122,44,17] Additionally, these are environmental-friendly technique, be it by enhancing the general energy effectiveness of the procedure or by diminishing the utilization of nonsustainable resources, decreasing ecological impression, while lessening handling costs and enhancing the added value of the product.[117] OH is generally known for its ability to give quick, homogeneous and exact heating wherever direct application of electrical energy to the food guarantees an exceptionally productive energy exchange. Thus, OH is as of now being effectively implemented in food handling industry.[133,131] More examinations have discovered that OHM has been appeared to build the extraction yields of rice grain oil and bioactive substances from rice wheat,[84,95] polyphenols from red grape pomace,[46] so on, as listed in Table 1.2.

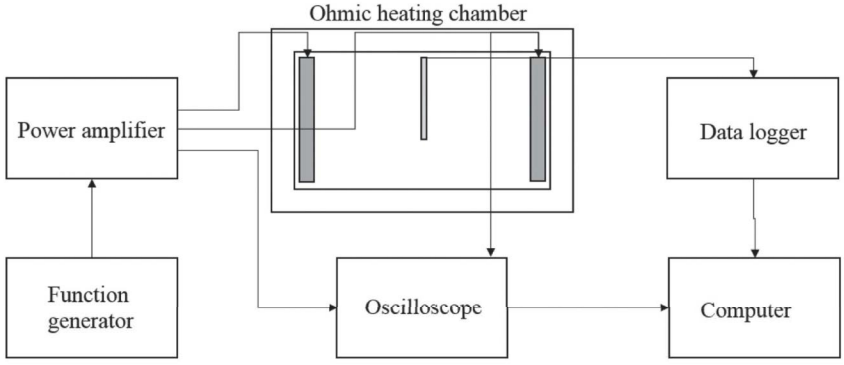


**FIGURE 1.6** Schematic diagram of high-frequency ohmic system.

**TABLE 1.2** Biomolecules Extraction by Novel Thermal Extraction Methods.

| Thermal method | Bioactive compound | Optimal conditions | Remarks | References |
|---|---|---|---|---|
| **Microwave-assisted extraction** | Oleanolic acid and Ursolic acid from *Ocimum sanctum* | Solvent: ethanol and methanol, power = 272 W time = 3 min, solid to solvent ratio = 1:30 | Highest extraction of OA and UA were observed with ethanol (89.64% and 86.76% | [142] |
| | Polyphenols from olive tree oil | Solvent free, power = 250–350 W, time = 2–3 min, amount of sample = 5–10 g | Both TPC and oleuropein were extracted at 250 W, 2 min, with 5 g sample | [130] |
| | Chlorogenic acid, caffeine and TPC from green coffee beans | Solvent: water, power = 800 W, time = 5 min, temperature = 50°C | Highest yield of chlorogenic and caffeine with MAE (31–62% and 22–40%, respectively) with radical scavenging activity of 75% | [145] |
| | Flavonoids from young barley leaves | Solvent: water, time= 11.12 min power = 1.27 W $g^{-1}$, liquid–solid ratio = 34.02 mL $g^{-1}$ | MAE extraction was more efficient than conventional, with maximum flavonoids yield of 80.78 ± 0.52% | [55] |
| **Ohmic heat-assisted extraction** | Anthocyanins from black rice bran | MC = 30% and 40%, electric field strength = 50–200 V $cm^{-1}$ | Both low and high concentration bioactive compounds were extracted. The highest level of bioactive compounds were observed at OHM with 40% MC ($E$ = 50, 100 , and 150 V $cm^{-1}$) and 30% MC ($E$ = 100, 150, and 200 V $cm^{-1}$) | [96] |

**TABLE 1.2** *(Continued)*

| Thermal method | Bioactive compound | Optimal conditions | Remarks | References |
|---|---|---|---|---|
| | Polyphenols from red grape pomace | Electric field strength = 100–800 V/cm, ethanol in water e/w = 00–50% | Cell membrane denatured to maximum extent. The highest extraction yields were obtained at 400 V/cm followed by a diffusion step for 60 min at 50°C and with a solvent composed of 30 % of e/w | [46] |
| | β-carotene and lycopene from gacaril oil | Electrical field strengths = 5.6 and 11.2 V/cm, garlic powder to n-hexane solvent = 1:7 (7 h), 1:6 (6 h) and 1:5 (5 h) | Highest extraction efficiency (81.40%) in ohmic treatment as compare to conventional | [1] |
| | Anthocyanins & total phenolic content from colored potato | Electric field strength = 0–30 V/cm, temperature = 30–90°C, Time = 0–10 min, water-based solvent | High recovery yield with less energy consumption, reduced treatment time, and no utilization of organic solvents | [117] |

MAE, microwave-assisted extraction; MC, moisture content; OA, oleanolic acid; OHM, ohmic heating, TPC, total phenolic content; UA, ursolic acid.

## 1.5.2 NONTHERMAL EXTRACTION METHODS

### 1.5.2.1 ULTRASOUND-ASSISTED EXTRACTION

The improvement of ultrasound innovation is not new but the fact is that in recent times, the developments in the utilization of power ultrasound have seen to be accomplished.[138] In this sense, particular consideration has been given to its utilization in the recuperation of bioactive compounds from various plants sources.

UAE of polyphenols is a nonconventional procedure that includes blending the specimen with organic solvent in a beaker and setting it in an ultrasonic bath with preset time and temperature (Fig. 1.7). Its better extraction effectiveness is identified with the phenomenon of acoustic cavitation. At the point when the ultrasound power is adequate, the sound waves traveling in rarefaction and compression cycles can develop microbubbles in the fluid. Once framed, bubbles will assimilate the vitality from the sound waves and develop during the extension cycles and recompress during the pressure cycle. Further, bubbles may begin another rarefaction cycle or fall driving stun influxes of extraordinary states of weight and temperature (about 1000 atmosphere and around 4000 K of temperature).[47,138,88] Subsequently, the bursting of cavitation bubbles produces microjets of liquid which can hit the surface of the plant matrix stimulating extraction of bioactive compounds from the specimen to the solvent medium.[38]

UAE has been proposed as an extroverted alternative to conventional extraction, furnishing higher recuperation of focused compounds with less utilization of solvent as well as quicker analysis of bioactivity properties. Mostly, the UAE procedure term is under 60 min; however, the extraction yield is 6–35% higher than that acquired utilizing conventional extraction methods with longer extraction time of at least 12 h.[147,69] These days, UAE is broadly utilized for the extraction of valuable compounds. For instance, it has been utilized for the extraction of oil[3], proteins,[124] polysaccharides-protein complex,[29] sugars,[75] etc. However, the extraction of antioxidants, for example, polyphenols has been uniquely tended to enhancing their recuperation based on their yield and antioxidant potential through experimental design. Table 1.3 shows a portion of the cases of bioactive particles separated by UAE.

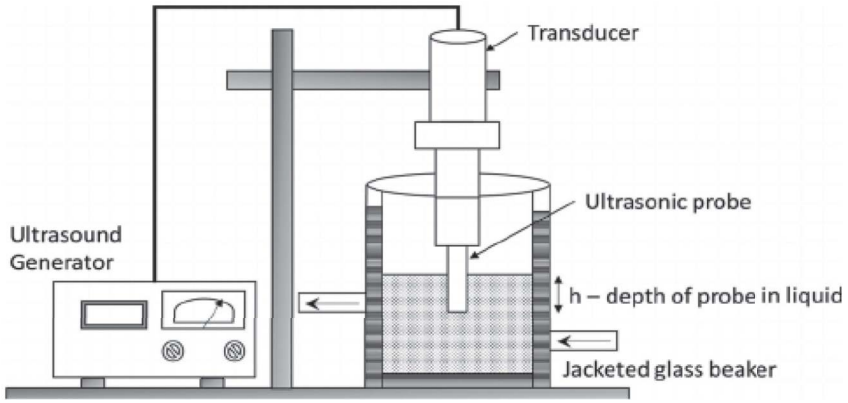


**FIGURE 1.7** Schematic diagram of ultrasound-assisted extraction using a probe system.

### *1.5.2.2 PULSE ELECTRIC FIELD-ASSISTED EXTRACTION*

The pulsed electric field (PEF) technique was perceived as valuable for enhancing the drying, dispersion, and pressing in the previous decade.[150,10,149] PEF is a rising innovation in recent years that has increased interest in the food industry for enhancing mass transfer operations.[123,81,44] The procedure depends on the utilization of external electric fields that instigate the electroporation of eukaryotic cell layers, improving the dispersion of solutes (Fig. 1.8). This permeabilization of cell membranes can be accomplished at moderate electric fields. PEF treatment includes the utilization of brief length (from μs to ms) electric field pulses of direct force (0.5–10 kV/cm) to plant tissues set between two anodes, causing the permeabilization not just of the cell membrane[19] but also of cell vacuoles[49] where a few metabolites are contained. PEF can destroy the layer structure of plant material thus expands mass exchange during extraction for improving extraction and diminishes extraction time. PEF has been connected to enhance arrival of intracellular components from plant cell by increasing permeability of cell membrane.[144] PEF application at a direct electric field (500 and 1000 V/cm; for $10^{-4}$–$10^{-2}$ s) is seemed to harm cell layer of plant tissue with little temperature increment.[49,86] Because of this reason, PEF can limit the debasement of heat-sensitive compounds.[4] PEF

is additionally appropriate on plant materials as a pretreatment procedure preceding customary extraction to bring down extraction exertion.[94]

In particular, the upgradation in the extraction yield of phenolic compounds, anthocyanins, flavonoids, sugars, and proteins from food processing and agricultural by-products of various food commodities has been accounted for when PEF-assisted extraction with solvents has been utilized; some of them are mentioned in Table 1.3.

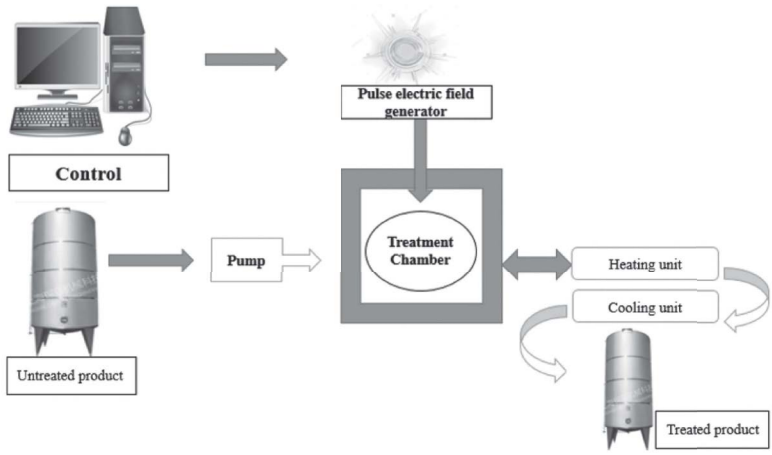


**FIGURE 1.8 (See color insert.)** Schematic diagram of pulsed electric field-assisted extraction.

### *1.5.2.3 SUPERCRITICAL FLUID EXTRACTION*

Supercritical state is achieved when a substance is subjected to pressure and temperature beyond its critical point. Critical point is characterized as the characteristic pressure (Pc) and temperature (Tc) above which particular gas and fluid stages do not exist.[67] This is the most mechanically propelled extraction framework.[116] Supercritical fluid extraction (SFE) includes utilization of gases, typically $CO_2$, and compacting them into a thick fluid. This fluid is then pumped through a barrel containing the material to be separated. From that point, the concentrate-loaded fluid is drawn into a partition chamber where the concentrate is isolated from the gas and the gas is recuperated for reutilization (Fig. 1.9). Solvent properties of $CO_2$ can be controlled and balanced by shifting the pressure and temperature

that one works at. The upsides of SFE are the adaptability it offers in pinpointing the constituents you need to separate from a given material and the way that your finished result has for all intents and purposes—no solvent deposits left in it. Supercritical carbon dioxide ($SC–CO_2$) is an appealing contrasting option to natural solvents since it is economical, nonexplosive, nontoxic, and has the capacity to solubilize lipophilic substances, and can be effortlessly expelled from the last items.[129,156,155] The drawback is that this innovation is very costly. There are numerous different gases and fluids that are exceedingly productive as extraction solvents when put under pressure.[116]

Nowadays, SFE is tremendously utilized as a part of numerous modern applications including coffee decaffeination, unsaturated fat refining and the extraction of fundamental oils and flavors from characteristic sources with potential use in functional foods and nutraceuticals.[39] This technique is a vital option over regular conventional extraction strategies utilizing organic solvents for extricating biologically dynamic compounds.[155] In any case, to build up an effective SFE, a few components should be taken into mind including SFs, cosolvents, crude materials, and extraction conditions for the extraction of a specific compound of interest in order to augment the extraction.[24] A few investigations have depicted the extraction of various common bioactive compounds utilizing supercritical liquid in Table 1.3.

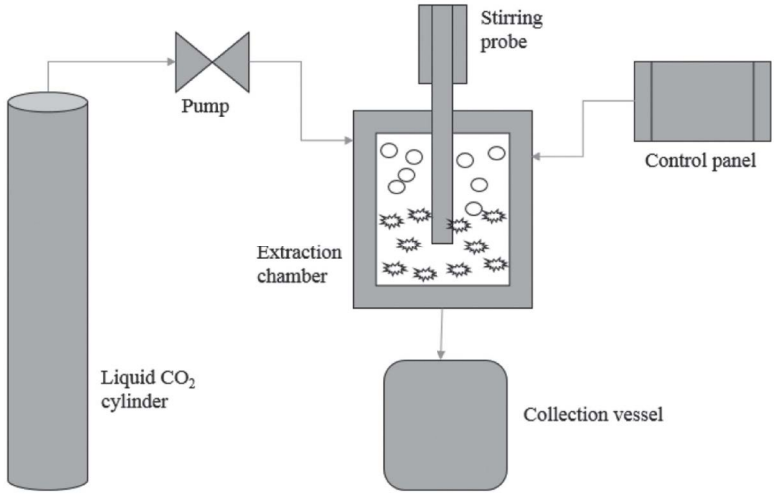


**FIGURE 1.9** Scheme of a supercritical fluid extractor plant.

### 1.5.2.4 HIGH-PRESSURE-ASSISTED EXTRACTION

High-pressure processing is a food processing strategy that has indicated extraordinary possibilities in the food industry. Like heat treatment, high pressure can also be useful in denaturation of proteins, inactivation of microorganisms, and increasing the shelf life of processed items.[21,93] The utilization of high-pressure treatment in the extraction of bioactive compounds from plant material is a new strategy, which has been known as ultrahigh pressure extraction (UPE)[73] or high hydrostatic pressure extraction (HHPE).[159] The studies demonstrated that high-pressure system could abbreviate processing time, get higher extraction yields, utilization of lower power, have fewer impurities in the extraction fluid, and have no negative impact on the movement and conformation of bioactive segments.[33] Most importantly, this extraction method could be worked at ambient temperature with no thermal procedure, aside from the temperature rise occur because of the pressure.[32,132] UPE works at high pressure (normally 100–600 MPa) and low temperatures (generally up to 60°C) to extricate rapidly with low volumes of natural solvents and gives recuperations like other different techniques.[165] Parameters that essentially influence these recuperations are temperature, pressure, solvent, the number of cycles, extraction time, etc.[28] Every parameter can be advanced independently or by utilizing an experimental design (Fig. 1.10).

The pressure difference between inside and outside of the plant material system is extensive under HPE conditions. This pressure difference can pervade the solvent to move quickly through the broken films into plant material and enhance the mass transfer rate of solute or the rate of disintegration, which prompts reduced extraction time utilizing HPE, contrasted with ordinary extraction forms.[164] Besides, HPE can inactivate degrading enzymes, which may clarify the greater extraction yield and antioxidant activity as compared to other conventional extraction methods.[5] High pressure likewise can diminish the pH of the solvent during extraction and this decrease may improve the extraction of bioactive molecules because these are steadier at low pH.[93,78,33,13]

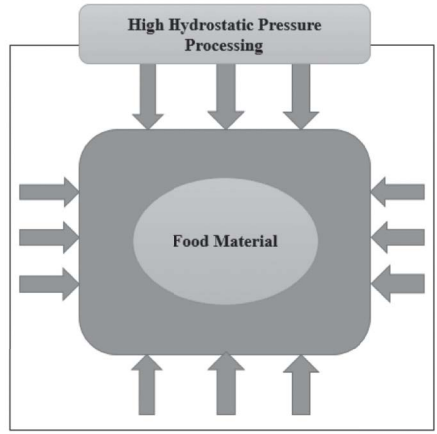


**FIGURE 1.10** **(See color insert.)** Schematic diagram showing mechanism of high-pressure system.

**TABLE 1.3** Biomolecules Extraction by Novel Nonthermal Extraction Methods.

| Thermal method | Bioactive compound | Optimal conditions | Remarks | References |
|---|---|---|---|---|
| **Ultrasound-assisted extraction** | β-carotene from *Spirulina platensis* alga | Solvent: n-heptane, temperature = 30°C, electrical acoustic intensity = 167 W/cm$^2$ | Ultrasonication showed 12 times increase in extraction yield of β-carotene (47.10%) | [43] |
| | Total phenols, antioxidant capacity, chlorogenic acid, caffeic acid, catechin, and epicatechin from carrot pomace | Solvent: ethanol 13–97%, time = 3–37 min, extraction temperature = 10–60°C | UAE decreases the extraction time and increases the extraction yield | [69] |
| | Fatty acids, b-sitosterol, a-tocopherol, squalene, total phenolics and carotene from palm pressed fiber | Solvent: ethanol, time= 2 h, temperature = 20 ± 2°C, electrical acoustic intensity = 36–204 W.cm$^{-2}$ | Bioactive compounds possessing antioxidant activity were identified and quantified | [40] |

**TABLE 1.3** *(Continued)*

| Thermal method | Bioactive compound | Optimal conditions | Remarks | References |
|---|---|---|---|---|
| **Pulsed electric field-assisted extraction** | Anthocyanins from purple-fleshed potato | Solvent: water 48% and ethanol 96%, time = 60–480 min, temperatures = 10–40°C, 5–35 pulses of 3 μs, 35 kV voltage | Extraction yield of anthocyanin increases by PEF at lower temperature with water as solvent | [121] |
| | Anthocyanins and flavonoids from plum and grape peels | Solvent: water, temperature = 70°C, 6 μs pulse width, 25 kV voltage | Chamber of larger diameter allows high number of pulses which helps in increasing the recovery of anthocyanins, flavonoids, and phenols from both fruits | [104] |
| | Anthocyanin from red cabbage | Solvent: water, 2.5 kV/cm electric field strength; 15 μs pulse | About 16–889 μg/mL anthocyanins were extracted, which are 2.15 times enhanced by PEF in water | [51] |
| **Supercritical fluid extraction** | Oleic acid, sterols and tocopherols from *Moringa oleifera* | Tempperature = 30°C, time = 300 min, pressure = 350 W, solvent/solid ratio = 1329.77 g $CO_2$/g | About 72.26–74.72% oleic acid (a health promoting fatty acid) is extracted | [127] |
| | Tocopherol from *Chenopodium quinoa* | Temperature = 130°C, time = 55–180 min, pressure = 185 W, solvent/solid ratio = 8.02–67.5 g $CO_2$/g | With comparison to hexane extraction, vitamin E yield increases four times by SFE | [120] |
| | Linolenic acid from *Gynostemma pentaphyllum* | Temperature = 43°C, time = 160 min, pressure = 320 W, solvent/solid ratio = 1483.11 g $CO_2$/g | About 95.69% of unsaturated fatty acids content was produced as compare to conventional methods | [154] |

**TABLE 1.3** *(Continued)*

| Thermal method | Bioactive compound | Optimal conditions | Remarks | References |
|---|---|---|---|---|
| **High pressure-assisted extraction** | Total phenolic, flavonoid, tannin and Antioxidant activity from fig | Solvent = ethanol 15–48%, time = 18 and 29 min, pressure = 600 MPa | High pressure led increase of 8–11% of total phenolics, flavonoids and tannins content and 8–13% of antioxidant activity when compared to extracts performed at 0.1 MPa | [8] |
| | Catechins from green tea | Solvent: ethanol 50%, time = 15 min, temperature = 20°C, pressure = 600 MPa | Extraction yield was greater in shorter time as compare to conventional reflux extraction method | [73] |
| | Lycopene from tomato waste | Solvent: ethyl lactate, time = 10 min, pressure 700 MPa | HP-assisted extraction led to higher yields (from 2% to 64% | [140] |

PEF, pulsed electric field; SFE, supercritical fluid extraction; UAE, ultrasound-assisted extraction.

## 1.6 SUMMARY

The efficiencies of either conventional or novel extraction techniques typically rely upon the basic input parameters: understanding the idea of plant lattice; chemistry of bioactive segments, and capability to up-scale them. Besides, choice of reasonable extraction process and advancement of different parameters are significant for upscaling purposes, that is, from bench scale to pilot plant level. Utilization of green extraction systems, for example, UAE,[105,92] MAE,[54] and SFE[113] has been quickly and constantly expanding all-inclusive for phytochemical handling of therapeutic plants as these strategies are quick when contrasted with conventional techniques. Likewise, these methods are ecologically amicable as far as energy and solvent utilization are concerned. Yield is likewise practically identical to traditional extraction and in some cases, it is much higher. Green

extraction systems other than enhancing the yield and quality would have the capacity to save time and energy.

## KEYWORDS

- **bioactive molecules**
- **terpenes**
- **alkaloids**
- **polyphenols**
- **Soxhlet**
- **liquid–liquid extraction**
- **maceration**
- **hydrodistillation**
- **ultrasound**
- **microwave**
- **supercritical fluid extraction**
- **pulsed electric field**

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