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Review Article

Bioactive Compounds - A New Era of Therapeutic Medicines

Disha Das*, Rojina Khatun, Sudeshna Sengupta, Malavika Bhattacharya

Department of Biotechnology, Techno India University, Salt Lake, Kolkata, India

Abstract

Bioactive compounds are secondary metabolites derived from plants. These secondary metabolites are present in plants, functioning in their metabolism and disease-resistance capacity. Herbal bioactive compounds are an emerging topic of research, opening a new sphere in the world of medical research. Since ancient times, these medicinal plants have been employed for the treatment of various diseases and for building up immunity. Herbally derived bioactive compounds are showing a new potential to treat different diseases, even communicable ones, along with certain incurable chronic illnesses like dementia and diabetes, and even promising cancer treatment. Different extraction methods are used, both innovative and conventional, for the isolation and identification of these compounds. Much research has been carried out over the years for the discovery of these compounds and their intervention in different therapeutic diseases. They have different applications in providing different therapeutic agents. For instance, alkaloids serve as chemotherapeutic agents providing treatment for cancer, and flavonoids are used for the management of neurodegenerative diseases. Limonene present in citrus seeds inhibits the growth of metastatic cells, boosting immunity. The presence of quercetin in onions and apples shows antioxidant properties by neutralizing reactive oxygen species. Gingerol present in ginger shows strong anti-inflammatory actions. Green tea, rich in epigallocatechin gallate, can affect several signaling pathways in cell survival and thus show anti-cancer activity. This literature review provides a brief insight into understanding the bioactive compounds derived herbally. Their different extraction processes like liquid-liquid extraction, microwave, chromatographic, and non-chromatographic techniques.

Keywords

Bioactive Compounds, Natural Products, Therapeutic Agents, Chemotherapeutic Agents

1. Introduction

In the modern world of ever-changing lifestyles, the increased risk of underlying diseases and chronic invisible illness threats is on the rise. Standing in such a situation, there is an increasing demand for therapeutic drugs with fewer side effects, and cheap and natural products. At this point, research showed the achievements of health benefits from herbally derived bioactive compounds and their promising potential to treat diseases, both communicable and chronic. These bio-active compounds are derived from secondary metabolites of plants, which have shown excellent therapeutic potential along with their dietary properties. They have been used for ages in traditional medicine and show remarkable health benefits, as well as help in reducing several disease risks. Several studies are being done to detect and identify these compounds and their mechanisms to use them for human benefits, as claimed since ancient times, though further clinical trials are needed to justify such statements. Apart from their therapeutic potential, they have other benefits like

*Corresponding author: dishadas9830@gmail.com (Disha Das)

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lower production cost, short treatment time, and fewer side effects of drugs. The usage of bio-active compounds needs to be very carefully evaluated and thoroughly checked for any toxicological properties, biological efficiency, easy availability, user safety, and any persistence of long-term effects on the user. The World Health Organization has given an estimation of about 20000 medicinal plants found in almost 91 countries, along with 12 countries having mega biodiversity. In this chapter, we shall focus on different bio-active compounds, their potential uses as therapeutic drugs, different extraction mechanisms used, their challenges, and prospects [1].

1.1. What Are Bio-active Compounds, and Why Are They Used

As noted, bioactive compounds are secondary metabolites found in abundance in plants. These medicinal plants consist of polysaccharides, phenols, polyphenols, terpenes, and alkaloids, which have been isolated, and they show numerous properties like anti-inflammatory, antioxidant, stress resistance, healing properties, and can even alter immunological pathways. They have even shown resistance to many chronic illnesses such as diabetes, cardiovascular disorders, and neurological disorders, and have even shown promising cures for cancer. Most of the compounds have shown anti-oxidative properties that in turn help in enhanced cell repair, comparatively less cell damage, and increased resistance towards oxidative stress. In short, bioactive compounds could be described as secondary metabolites derived from plants that show therapeutic or toxicological properties in humans and animals depending on their structure and function [2].

1.2. How Are Bio-active Compounds Extracted

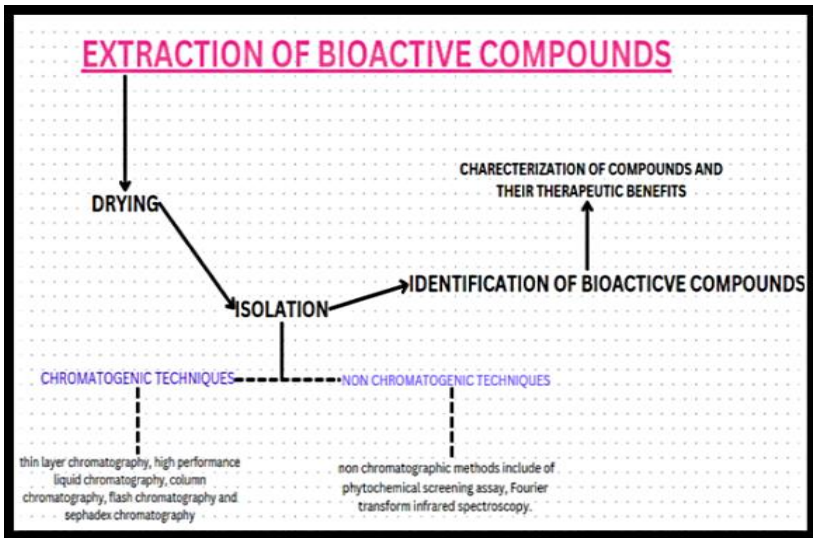

Figure 1. *Schematic Diagram Showing the Stepwise Procedure of Bioactive Compounds Extraction.*

The extraction of different bio-active compounds is one of the major areas of research, as more modern and efficient techniques are coming into rapid use in the extraction of complex bio-active compounds from different plants. This field is rapidly gaining popularity due to the rising demand for bioactive compounds in the food and drug industries. With such rising demand, further research procedures are immediately needed to overcome extraction challenges and the breakdown of complex bioactive molecule structures. Efficient extraction procedures implemented play an important role in the identification of phytochemical compounds as well as their yield. Stéphane [3]. Research has evolved modern extraction techniques with shorter extraction times, better preservation for thermolabile compounds, and less solvent consumption [4].

A. Some of the actively used modern methods include microwave-assisted extraction, surfactant-mediated techniques, solid-phase extraction, solid-phase microextraction, and supercritical fluid extraction. Sasidharan [5].

Apart from the extraction, isolating these bioactive compounds individually from their complex structure is also an important aspect of characterizing their properties. The first step for isolation comprises drying, which helps in the degradation of enzymes and the better preservation of plant materials. Drying could be achieved by sunlight, though not commonly preferred, as direct sunlight could cause unwanted chemical reactions due to ultraviolet radiation. The preferred method is to dry them at 40 - 50 Celsius in an oven.

The next step added is grinding or powdering of the plant materials to increase their surface area, increasing the contact between the sample and extraction solvents for faster as well as better yield of desired products. Conventional methods like

mortar and pestle, mills, and grinders are usually used to achieve the results [6].

The next step includes isolation of a complex mixture of bioactive compounds using chromatographic techniques. Isolating bioactive compounds of divergent structures and polarities is a great challenge to scientists. Many different chromatographic techniques, such as thin layer chromatography, high-performance liquid chromatography, flash chromatography, column chromatography, and Sephadex chromatography. Apart from these, some non-chromatographic methods include phytochemical screening assay and Fourier transform infrared spectroscopy. Out of the chromatographic techniques, the most widely used, vigorous, and adaptable technique is high-performance liquid chromatography. After the separation, these pure compounds are then used for identification and characterization. Extraction, isolation, and characterization of bioactive compounds from plant extracts [7].

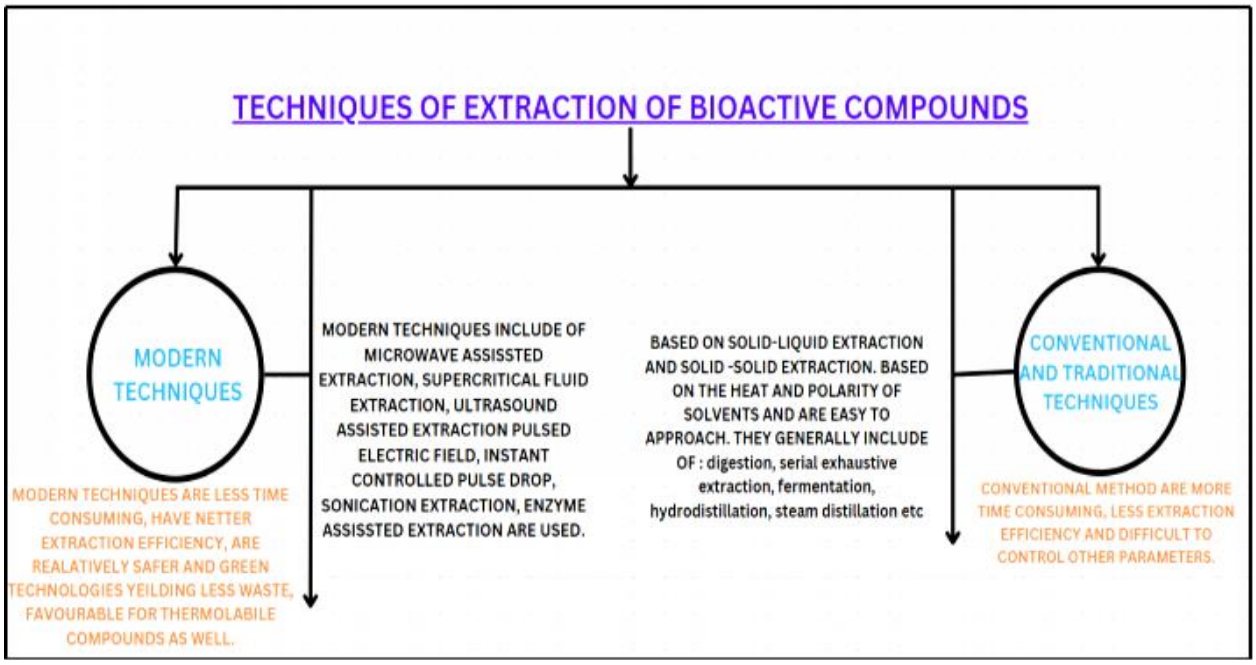

Figure 2. *A Chart Showing Different Techniques, Both Modern and Conventional, In Bioactive Compound Extraction.*

Many extraction techniques are used for high efficiency in the extraction process, Some conventional techniques are based on solid-solid or solid-liquid extraction, based on heat, polarity, and PH parameters. Some of them are digestion, serial exhaustive extraction, fermentation, hydro distillation, steam distillation, etc. Some recent researchers have developed innovative ways for extraction by using ultrasound and microwaves. Other techniques consist of supercritical fluid extraction, pulsed electric field, instantaneously controlled pulse drop, sonication extraction, enzyme-assisted extraction, etc. Furthermore, green solvent system development is a current topic of interest among researchers. The deep eutectic solvent is a new type of green solvent reported in 2003. This solvent consisted of a hydrogen bond donor as well as a hydrogen bond acceptor. It has high extraction efficiency, very high selectivity, and solubility, along with a harmonious nature. Apart from these, they have the advantage of being nontoxic and causing very little environmental pollution [8]. The most recent advance in extraction techniques is the use of abstract microwave techniques. Microwave techniques are more yielding, faster, stable, and less solvent-consuming. Microwave technology uses microwave energy for extraction. Bagade, S. B., &Patil, M. Apart from this, supercritical fluid extraction, ultrasound-assisted extraction, pulsed electric field, and instant controlled pulse drop are also widely used techniques. These techniques are less hazardous green technologies that yield less wastewater [9].

2. Use of Nanotechnology in the Extraction of Bioactive Compounds

The use of nanotechnology in the extraction of bioactive compounds has seen significant development in recent years. The use of nanotechnology dates back to the early 2000 s when researchers started developing nanocarriers, enhancing compound stability and targeted drug delivery. Nanocarriers have been shown to overcome the disadvantages of conventional herbal medicines, mainly the unavailability of bioactive compounds evenly and their failure in targeted administration [10]. The plant extracts are combined with their corresponding salts to create these nanoformulations, where the creation of a nanoparticle is indicated by a change in the color. The

reaction occurring is a redox reaction where the metal ions are nucleated during the first activation phase for the biosynthesis of nanoformulations. In the reaction, heat is an important aspect as nanoparticles smaller in size agglomerate to form more thermodynamically stable and larger nanoparticles. The reduction of the metal ions leads to the formation of various-shaped nanoparticles in hexagons, rods, and spheres [11].

Apart from medicines, they are an actively used instrument in cosmeceuticals. They have an excellent ability to penetrate the skin easily and more effectively, thus releasing active chemicals into the skin. Another beneficial advantage of nanoparticles is their ability to encapsulate bioactive compounds, thus helping in reducing toxicity to the healthy cells, but at the same time maintaining their efficacy against the targeted cells. In a nutshell, the development of nanoparticles has provided targeted delivery from plant extracts and retains the potential for enhancement of therapeutic applications [12].

2.1. Parameters Affecting the Extraction of Bioactive Compounds

1) Different extraction solvents are used for different bioactive compounds, as the solvent polarity should be like that of the solute for their homogeneous mixture.
2) The pH of the solvent
3) The temperature maintenance
4) The use of ultrasonic power and the frequency in the case of modern extraction techniques
5) The response surface method is one of the best approaches to evaluate the perfect conditions for the extraction and selection of solvents. Azmir et al.
6) The nature of different bioactive compounds is responsible for affecting the selection of their suitable solvents [13]. For example, polar solvents having lower boiling points, like acetone and ethanol, are required for the isolation of phenolic compounds.
7) Other compounds like sugars, amino acids, hydrophobic compounds, peptides, etc, need water extraction.
8) Neutral, basic, polar, and acidic compounds require ethanol extraction procedures [14].

2.2. Challenges of Extraction Processes

There are still a lot of challenges being faced in the efficient extraction of bio-active compounds.

1) Extraction from plants poses major challenges as they are difficult to isolate from their complex structures, leading to difficulty in characterization.
2) Conventional methods fail to yield optimum results. They result in the degradation of compounds, making them unstable as well as time-consuming procedures. The availability of these compounds is also a factor, basically from organisms in marine organisms.
3) The temperature and pH solvent used affect the compound yield; therefore, optimization of these factors significantly improves the yield.
4) There is a rapid need for newer green technologies with lower waste yields for extraction purposes and lesser energy consumption.
5) There is also difficulty in compound extraction using green solvents.
6) Usage of microwave and electric pulse fields leads to damage to biological compounds.

In a nutshell, further research is needed to modernize extraction techniques and to maximize yield efficiency. A combination of controlling factors of extraction and method improvement can lead to better yield [15].

3. Applications of Bioactive Compounds in Fields of Therapy and Human Health Benefit

Bioactive compounds serve as anti-fungal, antibacterial, Anti-cancer, anti-inflammatory, neuroprotective, antioxidant, anti-viral, and prevention of many chronic illnesses, namely cardiovascular diseases and diabetes [16]. Advancements in extraction techniques lead to more identification of therapeutically important drugs having potential health benefits, opening new sectors of drug discovery. Some examples of such compounds:

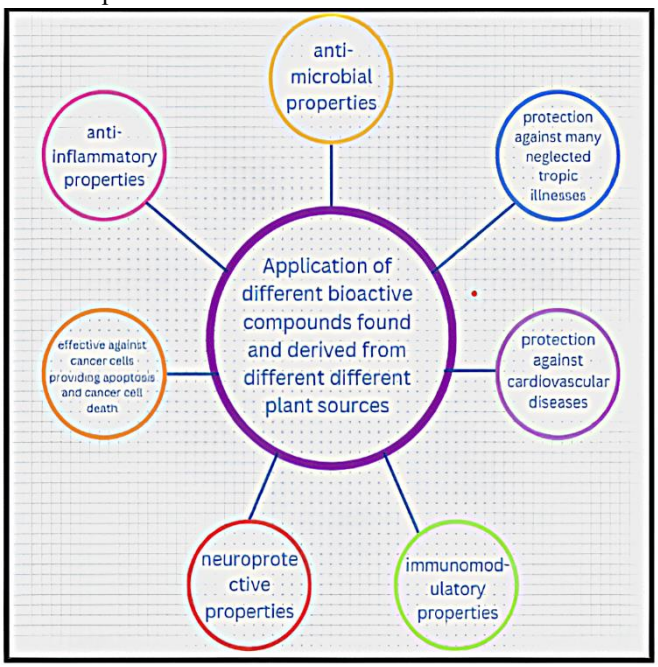

Figure 3. A Chart Showing Schematic Representation of Different Applications of Bioactive Compounds.

3.1. Antimicrobial

The mechanism of bioactive compounds against the microorganisms varies from different plant to another; some inhibit enzyme production or cell membrane lysis, leading to death. They are even shown to enhance the body's immune

response against harmful microorganisms.

1) A very common example of this is turmeric, used all over the world as a popular spice, showing antimicrobial functions. The presence of a yellow-colored compound called diferuloylmethane, commonly called curcumin. Turmeric has found its uses in spice, tea, food colors, and cosmetics [17].
2) Mung beans are also reported to show antimicrobial activities that target directly harmful microorganisms [18].
3) The presence of polyphenols like epigallocatechin gallate present in green tea works as an antifungal, preventing fungal growth like Aspergillus spp. and Candida spp.
4) Alkaloids such as sanguinarine from the Papaveraceae family and flavonoids like quercetin and kaempferol present in plants, camellia sinensis, and allium cepa show antibacterial properties.
5) Flavonoids like hesperidin show promising treatment against human immunodeficiency virus and influenza virus. In addition, these tannins present in green tea and pomegranate help in the prevention of hepatitis C virus and respiratory syncytial virus [19].

3.2. Antioxidant Properties

The presence of free radicals in the body is known to cause a variety of neurodegenerative diseases, cancer, aging, malaria, etc. So, antioxidant compounds that hunt for such free radicals are known to inhibit or rather reduce the risk of such diseases, thus calling for an extensive research policy [20]. Flavonoids like quercetin present in apples and onions show anti-oxidant properties, which inhibit lipid peroxidation while neutralizing reactive oxygen species.

1) Other polyphenols like resveratrol in grapes and curcumin in turmeric also help in reducing oxidative damage.

In 2018, research conducted on seed and leaves of wheat ethanol extracts showed high antioxidant properties of antioxidant thus proving the claim that plants help in human health benefits [21].

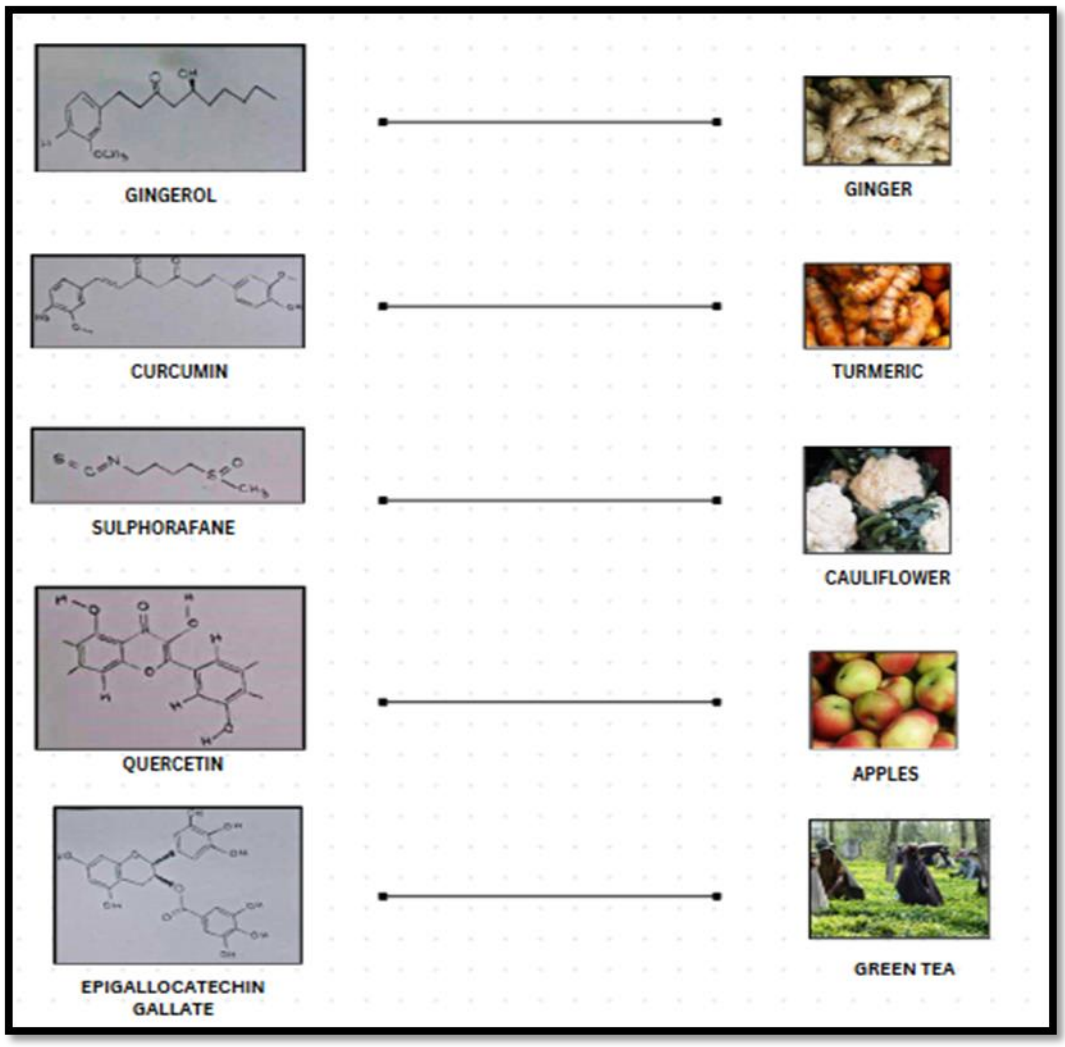

Figure 4. *Different Bioactive Compounds and The Plants They Are Derived From.*

3.3. Anti-Inflammatory Activities

This property works by inhibiting inflammatory regulatory factor inhibition or by decreasing inflammatory cytokines, namely tumor necrosis factor and interleukin-6.

Curcumin, as noted earlier, also acts as an active anti-inflammatory agent. It has a unique potential that inhibits the activation of an important inflammation regulatory factor called nuclear factor kappa-B.

Gingerol, found in ginger, also has strong anti-inflammatory effects.

Leaves of Glochidinacuminatum showed high anti-inflammatory effects in ethanol and total flavonoid content extracts [22].

3.4. Neuroprotective Properties

Neurodegenerative diseases are a major health challenge all over the world, finding their popularity in the aging population. Certain bioactives have shown potential in altering neural coordination, promoting brain health, and protecting against neurodegeneration.

Once again, curcumin from turmeric (Curcuma longa) excels, demonstrating potent neuroprotective benefits.

Extracts from the tobacco plants showed an inhibitory effect on NF-κB, an important activator in neuroinflammation. The presence of rutin showed major neuroprotective effects.

Bacopamonnier, commonly known as Brahmi, containing bacosides, has been shown to improve memory, reduce oxidative stress, and show benefits in Parkinson's and Alzheimer's disease.

Resveratrol, found in grapes, berries, and peanuts, has gained rapid popularity as it reduces amyloid-beta deposition, improving mitochondrial function.

Ginkgo biloba contains flavonoids and terpenoids showing positive benefits in treating cognitive diseases [23].

3.5. Immunomodulatory Activity

Some compounds have shown potential in regulating immune responses as well as providing immunity.

Ganoderma lucidum or reishi mushroom has polysaccharides, peptidoglycans, and triterpenoids.

The Echinacea plant contains alkamides that increase the activity of natural killer cells, T-cells, and macrophages [24].

3.6. Cardiovascular Functions

Shows unique benefits in regulating blood pressure and lipid profile.

Hawthorn or crataegus spp has flavonoids and procyanidins, improving blood flow and heart health, along with reducing cardiovascular damage.

Bioactive compounds derived over the years are effective against many neglected tropical diseases like chromoblastomycosis, scabies, leprosy, trachoma, trematodes, lymphatic filariasis, etc [25].

3.7. Against Cancer

Many bioactive compounds have been discovered showing anti-cancer properties of triggering cancer cell death, antiangiogenic properties, as well as limiting tumor development. Some of the compounds helpful are:

1) Polyphenols and resveratrol found in grapes and berries show strong effects on metastasis, cell proliferation reduction, apoptosis, and angiogenesis suppression. They have also shown evidence of reducing the side effects of chemotherapy and also in enhancing its capability.
2) Alkaloids such as vincristine and vinblastine, derived from Madagascar periwinkle against cancer, leukemia, and lymphoma. They have been shown to inhibit cell proliferation and apoptosis. Camptothecin blocks topoisomerase I, which is used in DNA repair and replication. It is derived from Camptotheca acuminata.
3) Terpenoids trigger apoptosis and cell proliferation.
4) Betulinic acid focuses on several signaling pathways that show involvement in cell proliferation and apoptosis. Certain compounds regulate gene expressions responsible for cancer, the regulation of the cell cycle, and cell apoptosis. Some compounds can activate the tumor suppressor pathway transcription factor FOXO3 a.
5) Compounds have also shown the ability to alter microRNA in cancer cells, leading to inhibition of tumor growth.

3.8. Compounds Containing Sulphur

1) Sulforaphane, found in cauliflower and broccoli, can trigger phase II detoxifying enzymes, which in turn reduce the growth of cancer cells.
2) Allium and garlic species contain isothiocyanate slows down tumor development and reduces metastasis [26].

3.9. Anti-diabetic Properties

Diabetes is a fast-advancing autoimmune disease responsible for increased death rates around the world, affecting individuals ranging from newborns to middle-aged and the elderly. The population is facing an extreme need for a safe and effective alternative drug for prevention as well as better management of diabetes. Many bioactive compounds have shown anti-diabetic benefits. Along with glucose level management, diabetes treatment also includes the prevention of long-term illnesses such as cardiovascular problems, kidney function, neuroprotective, etc. Some compounds are helpful:

1) Polyphenols found in different vegetables, fruits, and coffee show antioxidant properties that reduce oxidative stress responsible for the onset of diabetes.
2) Berberine, derived from Berberis vulgaris, contains al-

kaloids that help in altering gut microorganisms and improving insulin sensitivity.

3) Alkaloids help in managing diabetes by reducing the digestion of carbohydrates and reducing postprandial glucose levels by inhibiting enzymes like alpha-glucosidases and alpha-amylase.
4) Caffeine also helps by diminishing the risk of the development of type II diabetes [27].

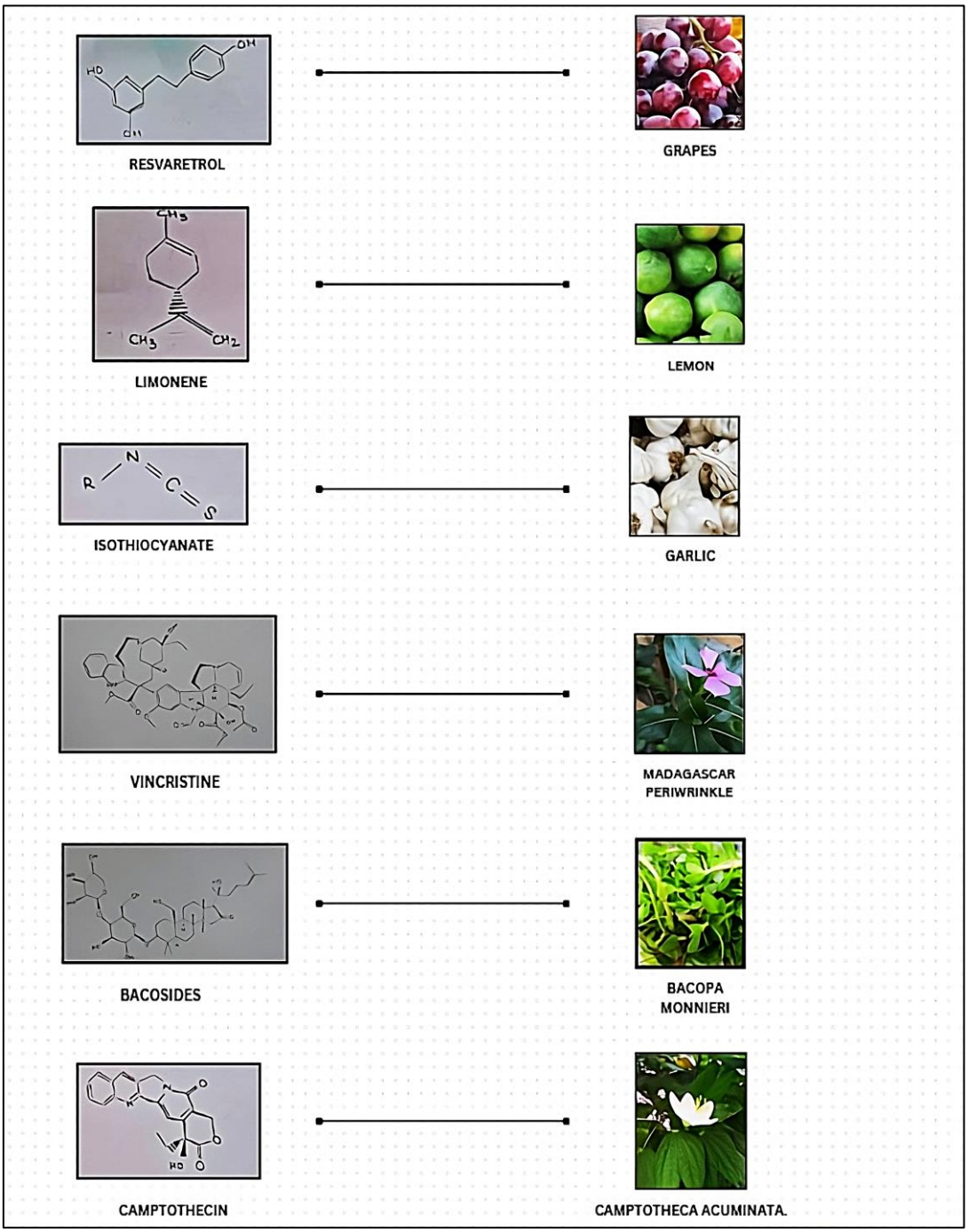

Figure 5. *Different bioactive compounds and the plants they are derived.*

3.10. Bioactive Compounds in Treating Different Chronic Illnesses

Bioactive compounds like terpenes and flavonoids from citrus compounds have shown promising treatments against chronic venous disease, which impacts many individuals globally but remains untreated and misdiagnosed [28].

2. Citrus hystrix DC or kaffir lime found in Southeast Asia has shown potential activity against treating Alzheimer's disease as these metabolites from kaffir lime targeted the

Alzheimer-associated genes with citrusoside and oxypeucedanin. Levodopa from Vicia faba or broad bean has shown promising results against Parkinson's disease [29].

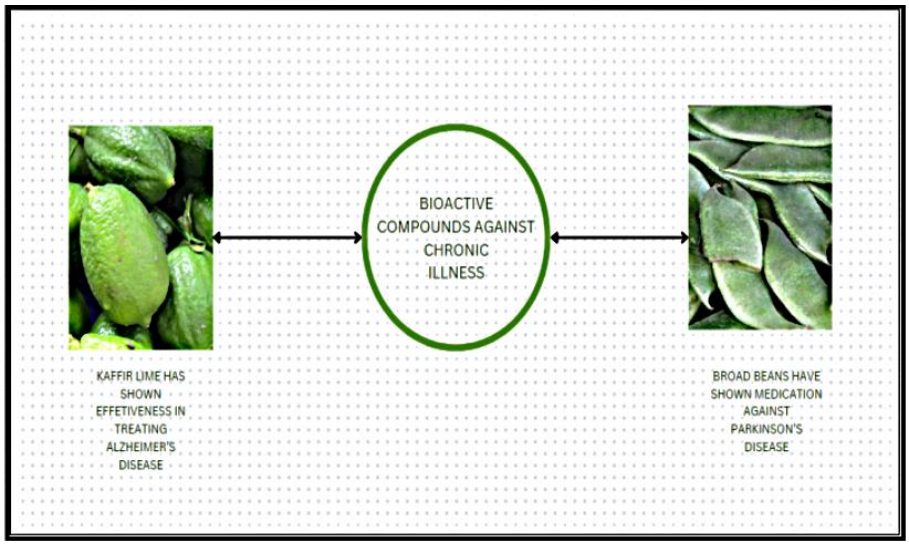

Figure 6. *Plants showing effectiveness against different chronic illnesses.*

Table 1. *Different amounts of the herbal compound present.*

Name of the herbal plant	Name of the herbal compound present	Amount of the herbal compound present
GRAPES	RESVARETROL	4,4 to 7,0 mg / dm³ (Balanov et al., 2021)
GINGER	GINGEROL	0.65-0.88% in green ginger and 1.10-1.56% in dry ginger (Chen et al., 1986)
TURMERIC	CURCUMIN	Pure turmeric powder can contain up to 3.14% (Tayyem et al., 2006)
GREEN TEA	EPIGALLOCATECHIN GALLATE	In Indian cultivars, EGCG levels range from 1.2% to 6.88% (G. Longo et al., 2008).
APPLES	QUERCETIN	Apple peels contain significantly higher levels of quercetin (253.57-744.59 µg/g) compared to the pulp (3.11-10.78 µg/g) (Mao et al., 2005)
LEMON	LIMONENE	Its concentration varies depending on the extraction method and fruit ripeness. In lemon peel oil, limonene content can range from 26.9% to 97.83% (Wani et al., 2021).
BRAHMI	BACOSIDES	C. Bramhi contains bacopaside I (5.37%), bacoside A3 (5.59%), bacopaside II (6.9%), bacopasaponin C isomer (7.08%), and bacopasaponin C (4.18%). B. Thorat, Ta Bagkar, R. Patil2018

4. Challenges Faced in Utilizing Bioactive Compounds

1) Quality control and standardization of these compounds are a major challenge. There are different methods of growing and harvesting plants containing these bioactive compounds, which can alter their chemical composition. There is a need to standardize the harvesting protocols to produce consistent qualities of products.
2) Toxicity evaluation is also a very important aspect; some bioactive compounds can show adverse effects and can be harmful to human consumption. A thorough evalua-

tion is needed to stop such occurrences before utilizing them as therapeutic agents.

3) The availability of compounds uniformly is also very difficult due to poor absorption, low solubility, and rapid metabolism.
4) Though evidence suggests that bioactive compounds are effective therapeutic agents, more clinical research is needed to determine their safety, usage, and potential in the drug industry [30].

5. Recent Advances in Bioactive Compound Research

1) Bioactive compounds can be used to address new diseases that remain unresolved by synthetic drugs.
2) The vast diversity of herbal compounds needs identification for the development of therapeutic drugs.
3) New research is needed to improve discoveries, extraction procedures, and bioassays.

6. Conclusion

Bioactive compounds are rapidly gaining interest for their huge usage in therapeutic benefits, leading to a new path in the drug industry with cheaper, safer, and a wider range of drugs available for a variety of diseases. New-age research procedures lead to fast discoveries of new-age extraction procedures, leading to better isolation procedures. For so many ages, humankind has been dependent on these natural sources of medicines. But with benefits comes a great responsibility of safeguarding this vast biodiversity of plants, providing these therapeutic compounds, which is an active need for their conservation for future use. Further research will help in safeguarding the clinical trial of these compounds, not only in clinical trials, as bioactive compounds have also found their use in the vast food industry to increase the benefits of different foods consumed. Thus, marking a new era of clinical research and drug development.

Abbreviations

ABCs	Antibiotic Bioactive Compounds
Bas	Bioactive Agents
BCPs	Bioactive Compounds and Peptides
BDNF	Brain-Derived Neurotrophic Factor
CAPE	Caffeic Acid Phenethyl Ester
CBD	Cannabidiol
CQA	Caffeoylquinic Acids
CUR	Curcumin
EGCG	Epigallocatechin Gallate

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Author Contributions

Disha Das: Data collection, Formal Analysis, Writing - Original Draft
Rojina Khatun: Resources, Writing – Editing
Sudeshna Sengupta: Resources, Writing – Editing
Malavika Bhattacharya: Conceptualization, Supervision

Conflicts of Interest

The authors declare no conflicts of interest.

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