Review Article

A comprehensive review of novel bioactive compounds: Phytochemical diversity and therapeutic potential

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Abstract

In plants, bioactive compounds are best described as secondary metabolites having the ability to elicit pharmacological or toxicological impacts in humans and animals and are not essential for plant growth. The chemical constituents produced by most species of plants arise from their normal physiological processes. The primary metabolism includes all the biological pathways needed for the viability of plant cells, whereas the secondary metabolism involves the anabolism and the catabolism of compounds essential for the plants. These metabolites are utilized in drug and environmental fields along with wide commercial and nutraceutical products. As a consequence, secondary metabolites are produced in lower volume but serve as higher commercial value for bioactive compounds such as pharmaceuticals, fragrances, etc. This review provides a comprehensive description of primary and secondary metabolites; the diversity of bioactive compounds found in a plant species; and future aspects, thus establishing a framework for future research investigations regarding the therapeutic uses and commercial advancements of these bioactive compounds.

Keywords: Bioactive compounds, primary metabolite, secondary metabolite, therapeutic effect

Introduction

Bioactive compounds from the natural sources have become a keen interest of researchers in the recent years. Scientific works in ethnobiology in the upcoming biological fields such as traditional and modern scientific aspects is on the rise. We can say that there is a vast variety of such bioactive compounds since the plant biodiversity covers a large range. The term 'bioactive' is derived from Greek word (bios-life and activus-energetic). The various parts of plants which maybe nuts, whole grains, fruits, oil, vegetables, and so on, are the natural sources of these compounds. Primary metabolites are such compounds which directly participate in the functional and biological roles of a plant. The key primary metabolites essential for human survival are carbohydrates, proteins, lipids as well as vitamins (Simsek et al., 2024). Most of these bioactive compounds can be referred to as secondary plant metabolites. These secondary metabolites are not directly involved in the plants' growth but they are very much needed for the defense mechanism of the plants. Most of

these bioactive compounds are basically secondary metabolites having various potential properties such as antioxidant, antimicrobial, anti-inflammatory, antiviral, antitumor, anticancer, etc. (Anwar et al., 2013). The bioactive compounds belong to different classes which are extracted from plant sources such as flavonoids, coumarins, carotenoids, terpenoids, phenolics, alkaloids, glucosinolates, etc. (Ahamad et al., 2019). These compounds have several health benefits including the anti-good properties which have therapeutic values. India is one such large producer of horticultural products like vegetables or fruits globally. But despite this fact, a very huge portion of these fruits and vegetables is wasted as pulps, peels, etc. in the process of juice extraction in the food processing industry. The medicinal plants for production of these bioactive compounds are more favored as they come from a natural source and prove to be environmentally friendly rather than the synthetic sources of drugs. Additionally, the knowledge coming from traditional medicines along with their therapeutic practices linked with these medicinal plants has helped in laying the foundation of today's modern drug advancements (Mushtaq et al., 2018). Furthermore, the native people have trusted long back on the therapeutic properties of medicinal plants, and their prior knowledge on traditional medicines has a positive impact to identify and utilize these novel bioactive compounds (Degu et al., 2024). A fact of concern that maybe observed by exploiting these medicinal plants for our modern drug discovery may affect in the extinction of these sacred plants as well as their endangerment. This issue can be resolved by usage of endophytic fungi as per several literatures mention as these fungi can colonize the plant tissues and the protection that they provide alongside they also are a good source of such novel bioactive compounds (Rodriguez et al., 2009). As these medicinal plants show a wide range of healing properties, the research-oriented interest has escalated in order to find out the novel bioactive compounds which are an aiding factor in mankind (Othman et al., 2019).

Importance of medicinal plants as sources of bioactive compounds

The occurrence of secondary metabolites as a novel bioactive compound is seen naturally in medicinal plants or microbes. The natural occurrence of such secondary metabolites in plants (gymnosperms and angiosperms) as well as microbe (fungi) proves to be valuable bioactive substances which are used majorly in medicinal or industrial applications. The secondary metabolites unlike the primary metabolites are not directly involved in survival and procreation, they are present in all organisms but their amount varies and differs from species to species (Nawrot-Chorabik et al., 2022). The vascular plants unlike animals are found to produce such secondary metabolites which are species-specific. Moreover, classification of certain substances as a primary or secondary metabolite is debatable. In some cases, the proper function of some metabolites has not yet completely understood. For example, in some tissues of trees, lignin is

known to be a secondary metabolite, but it may also be known as a primary metabolite due to its role in xylem development (Nawrot-Chorabik et al., 2022). Till date, the products of exotic trees as well as shrubs like flowers and fruits have been mainly the primary sources of these novel bioactive compounds and so the search of secondary metabolites from native plants is the current focus due to their easy accessibility. Plants are exposed to various biotic and abiotic stresses and these stresses are countered by plants by specific defense mechanisms to cope up with their growth and development. The biotic stress factors include bacteria, pests, insects, fungi, and viruses which are pathogenic. On the other hand, the abiotic stresses include temperature, light, UV radiation, water deficit, saline conditions, heavy metal stress, etc. The biotic stress factors enter in to the trees and woody plants along with pathogens, pests, etc. These plants have certain structures such as resins and waxes on the plant surface, or produce any other substances to stop the growth of the pathogen to create a barrier for the pathogens and pests. These substances produced are secondary metabolites for instance, phenolics, alkaloids, sesquiterpenoids, etc. Some of the secondary metabolites provide protection against the herbivorous insects (Carmona et al., 2011), fungi, and also bacteria which are pathogenic in nature. These novel bioactive compounds may cause synergistic effect or antagonistic effect in general. The inter-reactions between ascorbic acid, quercetin-3-rutinoside as well as 5-caffeoylquinic acid maybe influenced due to the absence of iron in thermal processing. It was found that the results of this antioxidant characteristic are influenced by their interaction with different molecules, minerals, etc. (Engelhardt et al., 2021). It is also found that peat or turf may have certain secondary metabolites which can aid in agricultural implementations. Analysis of light, brown, and black peat from Lithuania were examined as natural sources. Some considerable amounts of acetohydroxamic, glycolic acid derivatives were found in peat extracts (Jarukas et al., 2021). Kemboi et al., 2020 made a review on the traditional medicinal applications, triterpenoid compounds as well as the several pharmacological activities of *Euphorbia* spp. In the special issue, there is mention of *Carissa* spp. about their phytochemical, pharmacological as well as nutraceutical features. Sum total of 121 compounds was extracted from few species of *Carissa* plant. The important bioactive compounds extracted were coumarins, cardiac glycosides, terpenoids, lignans, and steroids which help in the pharmacological features of *Carissa* spp. (Dhatwalia et al., 2021).

Key bioactive compounds in medicinal plants

Broadly, the phytochemical diversity of plants is classified into three biosynthetic groups on the basis of their chemical structures and metabolic pathways (Nawrot-Chorabik et al., 2022). The three major groups are 1) Phenolics 2) Terpenoids 3) Nitrogen-containing compounds. These three groups are produced using the primary biosynthetic pathways which are Shikimate pathway,

Mevalonate pathway and Alkaloid pathway, respectively. The diversity of phytochemicals found in trees is discussed below in Table 1.

Table 1: List of different classes of phytochemicals, their source plants and applications

Class	Sub-Class	Source plants	Applications	Phytochemical(s)	Source(s)
Alkaloids	Quinoline	*Cinchona officinalis* L.	Biological-Anti-malarial Industrial-Bittering agent in food industry	Quinine	Hariyanti et al., (2022)
	Indole	*Camptotheca acuminata* Decne.	Biological-Cytotoxic agent in colorectal cancer Industrial-Scaffold for drug synthesis	Camptothecin	Qiao et al., (2022)
	Isoquinoline	*Phellodendron amurense* Rupr.	Biological-Anti-diabetic Industrial-Fluorescent probes	Berberine	Li et al., (2022)
Phenolics	Flavonoids	*Ginkgo biloba* L. *Quercus robur* L.	Biological-Capillary stabilizer Industrial-UV filter in cosmetics	Quercetin, Catechin, etc.	Kuppusamy et al., (2016)
	Stilbenes	*Pinus sylvestris* L.	Biological-Anti-aging Industrial-Anti-fungal wood coating	Resveratrol, Pinosylvin, etc.	Verkasalo et al., (2022)
	Lignans	*Juniperus communis* L.	Biological-chemotherapy Industrial-Antioxidant	Podophyllotoxin	Doussot et al., (2017)
	Tannins	*Terminalia* spp.	Biological-Wound healing Industrial-Leather tanning	Gallic acid, arjunin, etc.	Saxena et al., (2016)

	Quinone	*Juglans regia* L.	Biological-Antimicrobial Industrial-Herbicides	Juglone, Lawsone, etc.	Solar et al., (2006)
Terpenoids	Monoterpenes	*Eucalyptus* spp. *Pinus* spp.	Biological-Anti-inflammatory Industrial-Fragrances	Alpha-Pinene, limonene, etc.	Kaur et al., (2012)
	Diterpenes	*Taxus brevifolia* Nutt.	Biological-Anti-cancer agent Industrial-Resins	Paclitaxel, etc.	Heinig and Jennewein (2009)
	Triterpenes	*Betula pendula* Roth	Biological-Selective apoptosis in melanoma cells Industrial-Emulsifier in drug delivery	Betulin, lupeol, etc.	Makhnev et al., (2012)
	Saponins	*Quillaja saponaria* Molina	Biological-Vaccine adjuvant Industrial-Natural foaming agent	Q-21	Fleck et al., (2019)
	Sesquiterpenes	*Santalum album* L., *Cedrus* spp.	Biological-Anti-skin cancer Industrial-Fixatives in perfumes	Santalol, Bisabolol, etc.	Misra and Dey (2013)
Others	Organosulfur	*Azadirachta indica* A.Juss.	Biological-Broad-spectrum antibiotic Industrial-Biopesticides	Allicin-like compounds	Kharwar et al., (2020)
	Lipids and waxes	*Quercus suber* L.	Biological-Drug delivery patches Industrial-Biodegradable sealants	Suberin, cutin, etc.	Simões et al., (2022)

Selection of plant species for bioactive compound screening

One of the important steps in the process of discovering therapeutic drugs extracted from medicinal plants is the selection of plant species for extraction, isolation and screening of bioactive compounds. As per literature, only 15% out of 250,000 higher plant species which are available were taken into account for screening of phytochemicals and ~6% species of plants were estimated for their biological features (Fabricant et al., 2001). Few approaches regarding screening of bioactive compound followed worldwide by researchers are being discussed below.

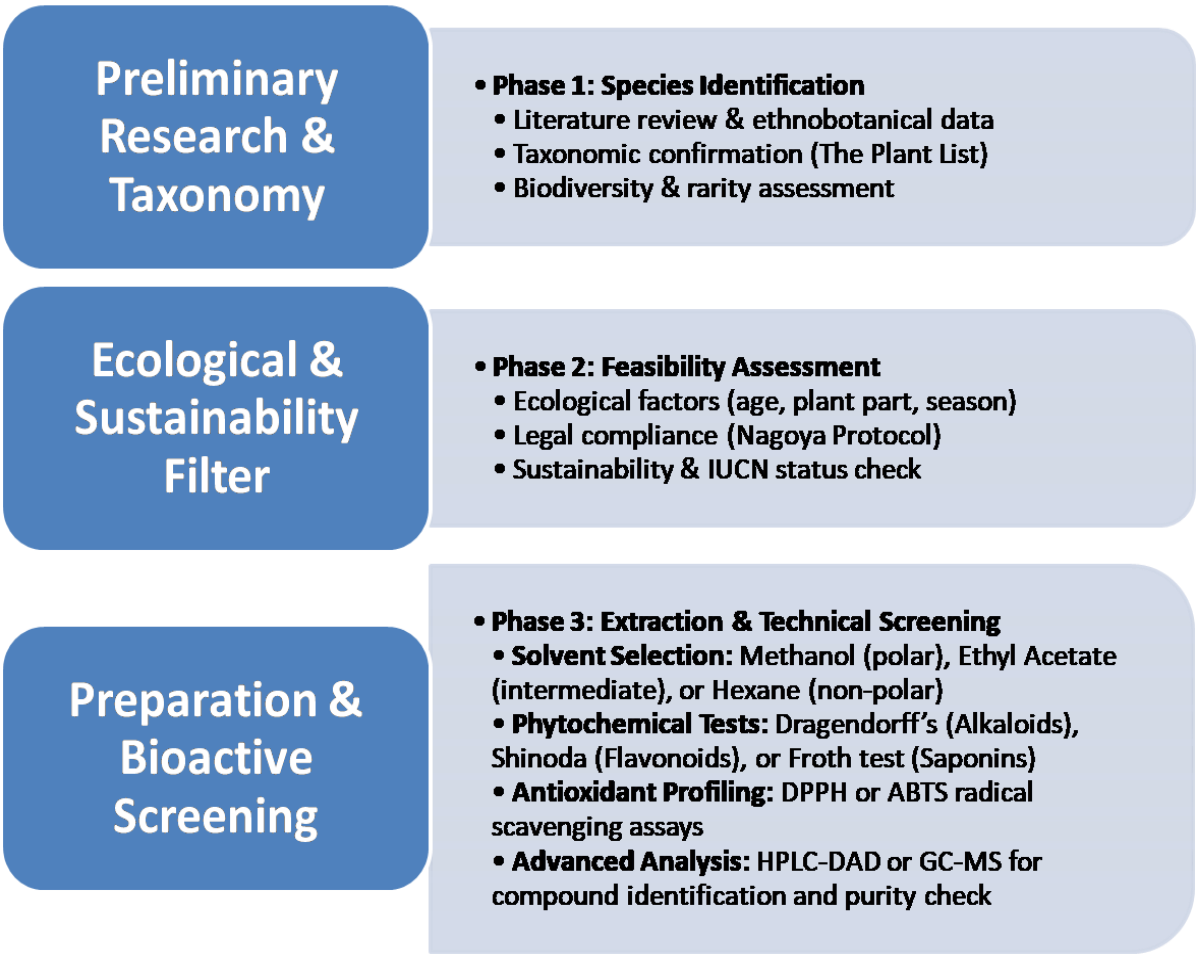

Figure 1: Flow chart explaining the selection of plant species for bioactive compound screening

Assortment based on ethno-pharmacological understanding: Utilizing this method for selection of plant for discovery of new bioactive compounds relies on the knowledge gained through observation related to the plant usage. This selection is based on tracing the traditional medicinal uses of flora through time. For instance, andrographolide was separated from the plant species *Andrographis* spp. and was used to cure dysentery in ethnomedicine. Furthermore, several

bioactive compounds such as berberine, picroside, morphine from the plant species *Berberis aristata* DC., *Picrorrhiza* spp. and *Papaver somniferum* L., respectively were separated based on this assortment. Based on observation, experimental evaluation, as well as description, the candidate plants are picked. (Katiyar et al., 2012).

Random approach: This approach involves picking the plants randomly from local or regional areas and then selected plants are screened for biological assays. Moreover, screening of certain target bioactive chemicals may also be done such as flavonoids, polysaccharides, alkaloids. This approach works for focused and general screenings alike, promising high success rates. The advantage of this random approach is that the plant candidates are easy to select, while the disadvantage includes that it does not give any pre-existing knowledge for bioactivity of the selected plant species.

Selection based on traditional medicine system: Some countries such as India, China have a rich culture of documentation of traditional medicines and are based on systematic framework of medicines from plant sources. The figure 1 describes the flow chart explaining about the discovery process of bioactive compounds.

This cataloged system is newer than the ethnomedicinal practices and different from ethnomedicinal practices in three ways:

i. These coded systems merged empirical practice with robust physiological theory, while the rest relied purely on practical experience.
ii. Traditional codified systems featured more sophisticated pharmaceutical formulations than ethnomedicinal practices, which basically relied on raw extracts like juices, decoctions and so on.
iii. Ethnomedicine is localized and controlled by a small group, whereas traditional medicine is well-institutionalized. Based on this approach, discovery of some of the important natural products are bacosides from *Bacopa monnieri* (L.), boswellic acid from *Boswellia serrata* Roxb., artemisinin from *Artemesia* spp., as well as reserpine from *Rauvolfia serpentina* (L.) are utilized as memory enhancer, anti-inflammatory, antimalarial and antihypertensive agents, respectively (Katiyar et al., 2012).

Future aspects

Scientific studies and discovery of these bioactive compounds are essential in depth so as to design next generation therapeutics which is based on such natural formulation. From several generations, these medicinal composition and formulations for the broad cure of diseases with proper selection and application are in use (Altaf et al., 2019). The future perspectives that need to be explored more about these novel bioactive compounds include creating standard phytopharmaceutical

formulations, pharmacogenomic methods and development of personalized medicinal strategies as well as working on developing a synergistic interaction of folklore medicines and modern science (Brindisi et al., 2020).

Conclusion

Due to the growth of polygenic disorders in the modern times, the notion of 'one disease, one drug' seems to have lost its sheen. Keeping these multi-disorders in mind, traditional medicines with multi-target therapeutic potential has been gaining significant interest in pharmacological industry. These novel bioactive compounds extracted from the medicinal plants provide a synergistic approach in solving such complex diseases in health system worldwide. The ethnopharmacological viewpoint analysis becomes fundamental because of the therapeutic activity which may be found in the chemo-diversity of these novel bioactive compounds. These therapeutic drugs worldwide are yet to be identified, analyzed and researched appropriately for the medicinal cure they behold for multi-diseases and thus this topic holds a great future in the scientific community.

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