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Review Article
Use of Plant Extracts in Alternative Medicine

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Abstract

Plants provide the oxygen required for maintenance of human life. They are essential for human life in terms of food and health. Thousands of years ago, humans explored the therapeutic power of plants and preferred to benefit from them to live healthily. According to the data of the World Health Organization (WHO), the number of plants used for therapeutic purposes is around 20,000. Since the beginning of using plants for human health, the bioactivity characteristics of the plants have been studied in laboratories. There are various bioactive components in plants, the most important of which are secondary metabolites. It is very important how and by which methods the secondary metabolites of plants are characterized as well as their isolation, proper and effective performance of their extraction process and identification of their various biological activities that might be used in alternative medicine. This review examines the usability of supplementary medical support products after the identification of bioactive characteristics of plants by means of various biochemical and molecular biological methods.

Key words: Plant, bioactive components, extraction, secondary metabolite, molecular biology

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INTRODUCTION

The most important source of natural drugs used in conventional treatment methods is plants. Research conducted worldwide during the recent years claim that almost 72,000 (corresponding to about 17%) of the 422,000 flowering plants which are spreading across the world have a therapeutic value[1]. In the 18th century, nearly 8000 plant species were classified systematically by Carolus Linnaeus (1707-1778) and this classification not only facilitated the works of naturalists but also the pharmaceutical chemists[2]. The science of ethnobotany, which deals with serious research recognized by all the world today, was born as a result of the bond that has existed between humans and plants for centuries. Ethnobotanic knowledge contributes greatly in the scientific evaluation of plants with its content that reflects very valuable information which was acquired by trial and error and has reached today via transfer from generation to generation over a long period of time[3]. The term "phytotherapy", that means "therapy with medicinal plants" was used by the French doctor Henri Leclerc (1870-1955) for the first time. Phytotherapy is one of the oldest natural therapy methods known in the human history, which aims to prevent and cure diseases with natural medications prepared by using all or some parts of the plants[4]. In this way, it was considered a strong possibility that bioactive substances which a plant species of well-known medical value contains, might be present in other plant species that are related with the former one and thus, the diversity of plants that can be used as herbal medicine has increased rapidly[5]. Plants convert, in their own metabolism, the water and minerals they get from the soil to nutrients that can be digested by the human body. Examples of the main nutrients include carbohydrates, proteins, lipids, vitamins and minerals[6]. These are commonly used active macromolecules that are produced in the plant's metabolism.

They increase the power of the defense of the body, support the functions of organs and/or accelerate recovery. Thus, they have a positive effect on the functions of specific tissues and organs in the organism[7]. Throughout human history, many diseases (diabetes, jaundice, shortness of breath etc.) have been tried and are still being tried to be cured by using plants. Scientists have conducted various kinds of studies for centuries to identify these therapeutic aspects[8]. The World Health Organization (WHO) has reported that about 4 billion humans around the world (80% of the world's population) try to cure their health problems with herbal remedies at the first step[9]. Furthermore, herbal active substances (vimbilastin, reserpine, kinin, aspirin etc.) make up around 25% of the prescription drugs in developed countries[10]. It was found in the literature that thousands of phytochemicals obtained from plants are reliable and have very few adverse effects. Many plants have been reported to exhibit anticancer, antimicrobial, antioxidant, antidiarrheal, analgesic and wound healing benefits[11,12]. There are many reasons behind the increase in studies conducted on plants. These reasons include frequent use of antibiotics that leads to pathogen micro-organisms' developing resistance and consequently, the reduction in the effects of antibiotics, the desire of developing countries that do not have a competent chemical industry of gaining an easy and economic treatment possibility, harmful adverse effects of the synthetic compounds used for therapeutic purposes, the fact that some substances that can be obtained from herbal drugs can be extracted more economically, easily and multiple effects of drugs[13]. These facts support the supplementary effect of herbal medicines on the organism when used in combination with synthetic drugs that are toxic and expensive and their use as an alternative means of treatment. Recently, detailed studies have been conducted to identify the bioactivity of extracts obtained from medical and aromatic plants with the aim of researching new compounds that control the oxidative DNA damage causing cancer[14].

In a study conducted by Moaket *et al.*[15] to identify the bioactive components of the endemic yellow iris plant, it was found that the plant had active components with antioxidant, antibacterial and DNA protecting properties. Plants with antimicrobial effects are of great importance in terms of controlling the organism species that develops resistance against the commonly used antibiotics[16]. The primary factor causing food spoilage and the loss of nutritional values is the microbial activity. Essential oils vary in their biological effects since they are complex compounds with different components[17]. While their effects change depending on their active substances, many essential oils have effects including antimicrobial, carminative, choleretic, sedative and diuretic effects[18]. Besides, essential oils of the aromatic plants, most of which belong to the Labiatae family have been shown to have antimicrobial activity[19]. For instance, it has been found that the essential oils of basil, laurel, clove, thyme and rosemary shows antibacterial activity against *Listeria monocytogenes* (*L. monocytogenes*) and other pathogens. It is claimed that garlic, cinnamon, curry, mustard, basil, ginger and some other plants exhibit antimicrobial effects[20]. In this study, the application of some chemical

methods used in isolation, extraction and characterization of the secondary metabolites, the most important bioactive components of plants, have been examined as well as some experimental methods used in identification of the bioactive component contents of the extracts obtained by using either biochemical or molecular biological methods.

Secondary metabolites of plants and how to obtain them: Plants produce proteins, lipids, carbohydrates and chlorophyll as the primary metabolic products after photosynthesis: Primary metabolites (carbohydrates, lipids, proteins, etc.) are quite common in nature and found quite a lot in the seeds and vegetative tissues of tall plants[21,22].

They are necessary for the physiological development of the plant due to their essential roles in the cell metabolism. Secondary metabolites, on the other hand are the chemical components that are not responsible for the growth and development of the plant but are generally believed to have roles such as adaptation to environmental conditions, chemical defense against micro-organisms, insects and other predators (hunters) and competition with other plants[17] (Fig. 1). The secondary metabolites that were previously assumed to have no role and be waste matter produced by the plants were discovered to be quite complex mechanisms developed by plants for defense, protection, adaptation, survival and continuity of the family purposes, in the 19th century[23]. These metabolites enable the plants to adapt to the biotic and abiotic stress conditions (against infection, injury, water, stress, cold and high intensity light)[22].

Secondary metabolites are hard to extract and purify since they are synthesized in specialized cell types of plants and different growth stages of plants[25]. Extraction, pharmacological screening, isolation and characterization of the bioactive substances with beneficial biological activity is extremely important. One of these process steps applied to obtain these metabolites from the plant under the most suitable conditions is as shown in the below Fig. 2[26].

Since the secondary metabolites are found in trace quantities in the plant, various biological and chemical technologies have been developed in recent years to obtain them. Extraction is the first step used in the process of drug research carried out on plants. In this very critical first step, efficient extraction of the chemical components from the plant material is necessary for their identification and proper separation in the following stages[27].

These extracts have various types of phytochemical or bioactive component combinations with various polarities, which allows serious efforts in the characterization of bioactive components. There are several separation techniques used commonly in practice to separate these bioactive components smoothly[28].

Some of these include column chromatography, sephadex chromatography, flash chromatography and HPLC. Apart from these, non-chromatographic methods such as immuno-assay and phytochemical imaging assay might also be used.

Biological methods used in the identification of bioactive characteristics of plants: Most of the bioactivity assessments are related to antimicrobial, antitumoral effects and the immune system[29]. There are various biological and biochemical and molecular biology based methods used in

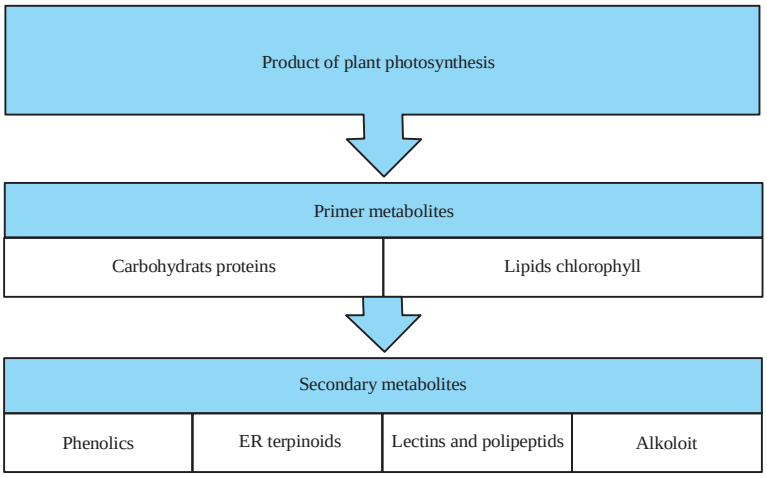

Fig. 1: Primary and secondary metabolites of plants[24]

Table 1: Antioxidant assay methods

Numbers	*In vitro* antioxidant test assay method
1	DPPH scavenging activity
2	Peroxynitrite radical scavenging activity
3	Hydrogen peroxide scavenging (H_2O_2) assay
4	Nitricoxide scavenging activity
5	Total radical-trapping antioxidant parameter (TRAP) method
6	Ferric reducing-antioxidant power (FRAP) assay
7	Superoxide radical scavenging activity (SOD)
8	Trolox equivalent antioxidant capacity (TEAC) method/ABTS radical cation decolorization assay
9	Hydroxyl radical scavenging activity
10	Hydroxyl radical averting capacity (HORAC) method
11	Reducing power method (RP)
12	Oxygen radical absorbance capacity (ORAC) method
13	Phosphomolybdenum method
14	Ferric thiocyanate (FTC) method
15	Thiobarbituric acid (TBA) method
16	Xanthine oxidase method
17	MPD (N,N-dimethyl-p-phenylenediamine dihydrochloride) method
18	β-carotenelinoleic acid method/conjugated die neassay
19	Cupricion reducing antioxidant capacity (CUPRAC) method
Numbers	***In vivo* antioxidant test assay method**
1	Ferric reducing ability of plasma
2	Reduced glutathione (GSH) estimation
3	Glutathione peroxidase (GSHPx) estimation
4	Glutathione-S-transferase (GSt)
5	Superoxide dismutase (SOD) method
6	Catalase (CAT)
7	c-Glutamyl transpeptidase activity (GGT) assay
8	Glutathione reductase (GR) assay
9	Lipid peroxidation (LPO) assay
10	LDL assay

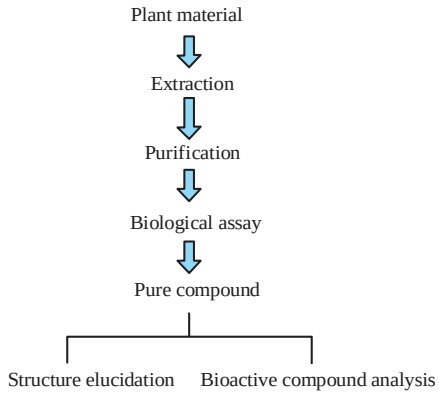

Fig. 2: A diagram of general approach on isolation, characterization and extraction of bioactive components from the plant extracts

the identification of bioactive characteristics of plants. Both *in vivo* and *in vitro* assessments are used in the identification of the biological activities of plant extracts[30]. All *in vivo* methods involve the use of micro-organisms and tests are applied on animals (mice, rats etc.) with proper doses and methods, followed by the assessment of blood or tissue samples. *In vitro* methods use sub-cellular systems such as enzymes and receptors that are isolated from animal or cell cultures[31]. The most commonly used one among these is the evaluation of the oxidant states of plants. Identification of the antioxidant activity in plant extracts is both an easy and cost-efficient method to be used in the elimination of the possible effects of the free radicals. Free radical types are required for cellular activities such as phagocytosis, regulation of cell proliferation, signal transmission, active component transfer and production of ATP[32]. Free radicals also have harmful effects. These harmful effects occur as a result of the irregularities between over-accumulation of free radicals and the anti-oxidant defense system. Therefore, free radicals must be neutralized[33]. Antioxidants are molecules that generally carry a phenolic function in their structure and protect the cell against damage by preventing the formation of free radicals or removing the existing radicals. Antioxidants significantly inhibit or delay oxidation of the substrate that is started with pro-oxidants in lower concentrations as compared to the substrates that can be oxidized[34,35].

Therefore, study of oxidant states in the extractions obtained after the required purification process while identifying the bioactivities of the plants is among the important biological and biochemical methods. There are 29 different methods in literature, including both *in vivo* and *in vitro* ones, which are used in the identification of antioxidant levels. As shown in Table 1, 19 of them are *in vitro* and 10 are *in vivo* assay methods[36,37].

According to the results of the study conducted by Alam *et al.*[38] the most commonly used 4 *in vitro* assays among these methods are DPPH>hydroxyl radical inhibitor>SOD>b-carotene>Linolate, whereas, the most common *in vivo* assay is LPO, followed by CAT, GSHPx. It is highly important to evaluate the DNA protection activities of plants while determining their antioxidant capacities. The methods to identify the DNA protection activity of plant extracts are among the most essential molecular biology methods. It is known that UV rays that reach the world due to the destruction of stratosphere layer have negative effects on the living beings. Antioxidants also provide protection against the harmful effects of UV rays. UV rays lead to severe diseases that result in skin cancer and aging. Topical application (on the skin) of enzymatic and non-enzymatic antioxidants is an effective approach in protection of skin against the harmful effects of UV rays[39,40]. Actually, human skin has a set of mechanisms that reduces the harmful effects of VIS (visible rays) and UV rays on human skin. But exposure to UV rays at a high level might lead to a decrease in the amount of cellular antioxidants and consequently UV-related oxidative DNA damage caused by reactive oxygen types.

Free radicals might also lead to DNA damage as well as the UV rays. For instance, hydrogen peroxide as a type of free radical, leads to DNA damage, by converting the guanine to 8 hydroxyguanine[41]. Recently, detailed studies have been conducted on extracts obtained from medical and aromatic plants with the aim of researching new compounds that control the oxidative DNA damage causing cancer[42].

CONCLUSION

As a result, it is highly important to elucidate the structure of plants used for centuries with the aim of both treatment and protection to prevent diseases. Many biological methods other than the ones we have mentioned in this review can be used to identify the bioactive characteristics of plants. Plant bioactivity elucidation studies are significant in the developing countries that do not have a competent chemistry industry since they provide an easy and economic treatment opportunity by benefitting from plants. Furthermore, discovery of harmful adverse effects seen in some of the synthetic substances that have been newly introduced in the medical treatment field has increased the need for using of less harmful natural products. Another advantageous aspect of the herbal medication is the increase in the resistance developed against antibiotics that are used for treatment against many micro-organisms which cause contagious diseases and hospital infections. Science has to synthesize and produce new and effective compounds or discovers natural products against the rapidly increasing resistance to the available antibiotics. Due to the high cost of production of new generation antibiotics, pharmaceutical industry needs to discover new antimicrobial substances and study the structures of these substances. We believe that biochemical and molecular analyses of secondary metabolites of plants that contain bioactive components will be highly enlightening in terms of usability of the extracts to be obtained from these components in the personalized alternative therapy methods.

Plant bioactivity studies serve as preliminary and supportive studies to elucidate the characteristics of plant extracts that might be used as the active substances of drugs in alternative medicine, especially in the field of pharmacology.

REFERENCES

1. Ojiezeh, T.I., M.I. Adarabioyo and P.T. Olagbemide, 2016. Phytochemical compositions of some extracts used in alternative medicine in Nigeria. Adv. Applied Sci. Res., 7: 1-6.
2. Charmantier, I., 2011. Carl Linnaeus and the visual representation of nature. Historical Stud. Nat. Sci., 41: 365-404.
3. Prance, G.T., 2007. Ethnobotany, the science of survival: A declaration from Kaua'i. Econ. Bot., 61: 1-2.
4. Capasso, R., A.A. Izzo, L. Pinto, T. Bifulco, C. Vitobello and M. Mascolo, 2000. Phytotherapy and quality of herbal medicines. Fitoterapia, 71: S58-S65.
5. Robbers, J. and V.E. Tyler, 1999. Tyler's Herbs of Choice: The Therapeutic Use of Phytomedicinals. Taylor & Francis, New York, USA., ISBN-13: 9780789001597, pp: 256-258.
6. Craker, L.E., Z. Gardner and S.C. Etter, 2003. Herbs in American fields: A horticultural perspective of herb and medicinal plant production in the United States, 1903 to 2003. HortScience, 38: 977-983.
7. Lahlou, M., 2004. Methods to study the phytochemistry and bioactivity of essential oils. Phytother. Res., 18: 435-448.
8. Eloff, J.N., 1998. A sensitive and quick microplate method to determine the minimal inhibitory concentration of plant extracts for bacteria. Planta Medica, 64: 711-713.
9. Lange, D., 2006. International Trade in Medicinal and Aromatic Plants: Actors, Volumes and Commodities. In: Medicinal and Aromatic Plants: Agricultural, Commercial, Ecological, Legal, Pharmacological and Social Aspects, Bogers, R.J., L.E. Craker and D. Lange (Eds.). Chapter 11, Springer, Netherlands, ISBN-13: 9781402054471, pp: 155-170.

10. Farnsworth, N.R., O. Akerele, A.S. Bingel, D.D. Soejarto and Z. Guo, 1985. Medicinal plants in therapy. Bull. World Health Organiz., 63: 965-981.
11. Greenwell, M. and P.K.S.M. Rahman, 2015. Medicinal plants: Their use in anticancer treatment. Int. J. Pharmacol. Sci. Res., 6: 4103-4112.
12. Desai, A.G., G.N. Qazi, R.K. Ganju, M. El-Tamer and J. Singh *et al*., 2008. Medicinal plants and cancer chemoprevention. Curr. Drug Metab., 9: 581-591.
13. Baytop, T., 1999. Therapy with Medicinal Plants in Turkey (Past and Present). 2nd Edn., Nobel Tip Kitabevleri, Istanbul, Turkey, ISBN: 9754200211, Pages: 342.
14. Moaket, S., S.B. Oguzkan, I.H. Kilic, B. Selvi and I.D. Karagoz *et al*., 2017. Biological activity of *Iris sari* Schott ex Baker in Turkey. J. Biol. Sci., 17: 136-141.
15. Grassmann, J. and E. Elstner, 2003. Essential Oils: Properties and Uses. In: Encyclopedia of Food Sciences and Nutrition, Caballero, B., P. Finglas and F. Toldra (Eds.). 2nd Edn., Academic Press, London, UK., ISBN: 978-0-12-227055-0, pp: 2174-2184.
16. Cowan, M.M., 1999. Plant products as antimicrobial agents. Clin. Microbiol. Rev., 12: 564-582.
17. Hammer, K.A., C.F. Carson and T.V. Riley, 1999. Antimicrobial activity of essential oils and other plant extracts. J. Applied Microbiol., 86: 985-990.
18. Hsieh, P.C., J.L. Mau and S.H. Huang, 2001. Antimicrobial effect of various combinations of plant extracts. Food Microbiol., 18: 35-43.
19. Alzoreky, N.S. and K. Nakahara, 2003. Antibacterial activity of extracts from some edible plants commonly consumed in Asia. Int. J. Food Microbiol., 80: 223-230.
20. Marino, M., C. Bersani and G. Comi, 1999. Antimicrobial activity of the essential oils of *Thymus vulgaris* L. measured using a bioimpedometric method. J. Food Prot., 62: 1017-1023.
21. Vanisree, M., C.Y. Lee, S.F. Lo, S.M. Nalawade, C.Y. Lin and H.S. Tsay, 2004. Studies on the production of some important secondary metabolites from medicinal plants by plant tissue cultures. Bot. Bull. Acad. Sin., 45: 1-22.
22. Theis, N. and M. Lerdau, 2003. The evolution of function in plant secondary metabolites. Int. J. Plant Sci., 164: S93-S102.
23. Materska, M. and I. Perucka, 2005. Antioxidant activity of the main phenolic compounds isolated from hot pepper fruit (*Capsicum annuum* L.). J. Agric. Food Chem., 53: 1750-1756.
24. Mulabagal, V. and H.S. Tsay, 2004. Plant cell cultures-an alternative and efficient source for the production of biologically important secondary metabolites. Int. J. Applied Sci. Eng., 2: 29-48.
25. Ozgen, M., F. Ertunc, G. Kinaci, M. Yildiz and M. Birsin *et al*., 2005. Tarim teknolojilerinde yeni yaklasimlar ve uygulamalar: Bitki biyoteknolojisi. Turkiye Ziraat Muhendisligi VI. Teknik Kongresi, January 3-7, 2005, Ankara, Turkey, pp: 315-346.
26. Morris, P. and M.P. Robbins, 1997. Manipulating Condensed Tannins in Forage Legumes. In: Biotechnology and the Improvement of Forage Legumes, McKersie, B.D. and D.C.W. Brown (Eds.). CAB International, UK., pp: 147-173.
27. Sasidharan, S., Y. Chen, D. Saravaran, K.M. Sundram and L.Y. Latha, 2011. Extraction, isolation and characterization of bioactive compounds from plants' extracts. Afr. J. Tradit. Complement. Altern. Med., 8: 1-10.
28. Fabricant, D.S. and N.R. Farnsworth, 2001. The value of plants used in traditional medicine for drug discovery. Environ. Health Perspect., 109: 69-75.
29. Huie, C.W., 2002. A review of modern sample-preparation techniques for the extraction and analysis of medicinal plants. Anal. Bioanal. Chem., 373: 23-30.
30. Zjawiony, J.K., 2004. Biologically active compounds from aphyllophorales (polypore) fungi. J. Nat. Prod., 67: 300-310.
31. Chikezie, P.C., C.O. Ibegbulem and F.N. Mbagwu, 2015. Bioactive principles from medicinal plants. Res. J. Phytochem., 9: 88-115.
32. Kinghorn, A.D., L. Pan, J.N. Fletcher and H. Chai, 2011. The relevance of higher plants in lead compound discovery programs. J. Nat. Prod., 74: 1539-1555.
33. Lobo, V., A. Patil, A. Phatak and N. Chandra, 2010. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn. Rev., 4: 118-126.
34. Halliwell, B., 1994. Free radicals and antioxidants: A personal view. Nutr. Res., 52: 253-265.
35. Karadeniz, F., H.S. Burdurlu, N. Koca and Y. Soyer, 2005. Antioxidant activity of selected fruits and vegetables grown in Turkey. Turk. J. Agric., 29: 297-303.
36. Chanda, S. and R. Dave, 2009. *In vitro* models for antioxidant activity evaluation and some medicinal plants possessing antioxidant properties: An overview. Afr. J. Microbiol. Res., 3: 981-996.
37. Badarinath, A.V., K.M. Rao, C.M.S. Chetty, S. Ramkanth, T.V.S. Rajan and K. Gnanaprakash, 2010. A review on *in-vitro* antioxidant methods: Comparisons, correlations and considerations. Int. J. Pharm. Tech. Res., 2: 1276-1285.
38. Alam, M.N., N.J. Bristi and M. Ra quzzaman, 2013. Review on *in vivo* and *in vitro* methods evaluation of antioxidant activity. Saudi Pharm. J., 21: 143-152.
39. Tepe, B., S. Degerli, S. Arslan, E. Malatyali and C. Sarikurkcu, 2011. Determination of chemical profile, antioxidant, DNA damage protection and antiamoebic activities of *Teucrium polium* and *Stachys iberica*. Fitoterapia, 82: 237-246.

40. Gutteridge, J.M.C., 1984. Lipid peroxidation initiated by superoxide-dependent hydroxyl radicals using complexed iron and hydrogen peroxide. FEBS Lett., 172: 245-249.
41. Wada, N., J.A. Cartagena, N. Khemkladngoen and K. Fukui, 2012. Bioactive bead-mediated transformation of plants with large DNA fragments. Methods Mol. Biol., 847: 91-106.
42. Vujcic, V., S.R. Brkanac, I.R. Redovnikovic, S. Ivankovic, R. Stojkovic, I. Zilic and M.R. Stojkovic, 2017. Phytochemical and bioactive potential of *in vivo* and *in vitro* grown plants of *Centaurea ragusina* L. detection of DNA/RNA active compounds in plant extracts via thermal denaturation and circular dichroism. Phytochem. Anal., 28: 584-592.