Review article
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Analytical techniques and herbal Medicinal Plants: A Review of past and present techniques

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Abstract
The present review deals with the qualitative and quantitative determinations of medicinal plants from classical to advance analytical methods. Medicinal plant analysis by different analytical viz., Spectroscopy, chrmatography, computational & spray drying methods have been reported and its essential to understand under current pandemic condition. Researchers are continuously engaged to find out the solution to overcome the problems caused by viruses like degue and COVID-19. Synthetic as well as natural remedies were applied to combat the spread of disease. Several drugs are obtained from natural resources which are utilized in controlling the disease. A piece of depth knowledge about the significance of medicinal plants towards healing, primary healthcare, and drug discovery is required using advanced technologies.

Keywords: Medicinal plants; Analytical Methods; HPLC; Spectroscopy; Spray Drying.

Highlights:
- Different analytical techniques utilized for useful component analysis served as medicine.
- Spectroscopy, HPLC, Computational and spray drying techniques were performed for separation, identification and preservation of herbal components.

1. Introduction
Plants are an important source for a broad range of foodstuffs that are imperative for human requirements. Plant resources are utilized for numerous functions together with wood, food, and medication (Cowan, 1999; Patwardhan et al., 2005). At present, approximately one-third of accessible medicines arrive from natural foodstuffs that have a plant source (Strohl, 2000). Currently, in pandemic condition of COVID-19 different medications were taken without consulting a physician (i.e. self medication). Self medication of analgesics, antipyretics, antitussives, antidiarrheals, calcium and vitamin supplements, anabolic steroids, sedatives, certain antibiotics, and many herbal and homeopathic remedies globally, affecting both developed and developing countries (Masood et al. 2020; Malik et al. 2020). Self medication of herbal medicine causing no more side effects as compare to rest of these medication.

Medicinal plants have shown great importance in healing, primary healthcare, and drug discovery (Fitzgeraldet al., 2019). Kadir et al. (2013) have repoted 13 different species of plants as a anti dengue agents by using their leaves, fruits and seeds (Lim, et al., 2021). Several researchers utilized different parts of plants for the treatment of COVID-19 (Lim et al., 2021; Khadka et al., 2021; Tariq et al., 2021; Adhikari et al., 2020; Nugraha et al., 2020) and found good results as shown in Table 1.

Chaachouay et al., (2021) have studied the 20 plant species which repeatedly used by herbalists of Salé Prefecture (herbal market) for the cure of COVID-19. Commonly, used plants were Eucalyptus globules Labill., Azadirachta indica , A. Juss,. and Ziziphus lotus, Lam.

In agreement with the current needs and supplies for drug manufacturing, the verification of analytical techniques or processes is the precondition for the composition of pharmacopoeial monographs development modifiable the quality testing of organic pharmaceuticals or plant origin. Consequently, it is essential to authenticate analytical methods for their proposed utilize in assessing the quality of the drug (Alekandrovna et al., 2019). The current review article deals with the qualitative and quantitative estimation of medicinal plants from classical to advance techniques.

Table 1. Medicinal plants utilized in COVID-19 and their phytochemical activities.

Medicinal plant	Phytochemical activity	Literature survey
Azadirachta indica, Eurycoma longifolia, Nigella sativa, V. amygdalinum	1) antiviral, 2) anti-inflammatory, 3)Immunomodulatory effects	Lim, et al., (2021).
Leaves of Coffea arabica (young) Coffea arabica (old) Psidium guajava Sauropus androgynus Tithonia diversifolia Mangifera indica Pandanus amaryllifolius Momordica charantia Euphorbiae hirtae Carica papaya Mimosa pudica Andrographis paniculata Piper ornatum Piper betle Annona muricata Anredera cordifolia Kaempferia rotunda Leucaena glauca Morinda citrifolia Coffea canephora (old)	1) antiviral, 2) anti-oxidant	Wulandari, et al., (2016).
Ecklonia cava (edible brown algae)	1) antiviral	Park, et al., (2013)

1.1 Quality control, identification, and expansion of herbal medicines (Official Pharmacopoeias)

There are several international pharmacopeias for herbal medicines and their raw materials, such as international pharmacopeia WHO (Ph. Int, WHO) (WHO Guidelines 2009), European Pharmacopoeia Ph. Eur. British Pharmacopoeia, United States Pharmacopeia, German-Japanese, Russian (Kiseleva et al., 2010), and Chinese Pharmacopoeia. Chinese Pharmacopoeia (ChP) 2015 is a complete & wide-ranging monograph. Consequently, the presented German-Japanese analytical methods were usually operated for the isolation of some medicinal compounds (Fitzgerald et al., 2019). Similarly, other pharmacopeias/monographs of the world covering all verities and species (raw plants, teas, slices, herbal mixtures, herbal drug mixtures, mixture herbal products, herbal collections, and oils are still utilized in approximately all conventional therapeutic system. (Hamid-Reza et al., 2013, 598; Qian et al., 2010; Yong et al., 2007; Che 2013).

1.2 Qualitative Analysis

Primarily, organoleptic or through physical senses method of analysis for medicinal plants were adopted during the period of the last seven decades, with the passage of scientific revolution progress of several most primitive analytical tools applied that were supporting the senses, the telescope, and microscope. These earliest analytical tools have great importance regarding the chemical, structural and atomic levels as the human perception has been broadened for sensitivity and range. Coming out of these analytical practicesin several features is equivalent to the sensory evaluation or organoleptic mixture that happens while picking the rapeutic plants by enhancing the peak of reference/arithmetical extent of freedom to get better the likelihood of suitably classifying and reviewing its quality. However, many new techniques and methods, especially the development of chromatographic and spectroscopic, have developed (Fitzgerald et al., 2019).

2. Analytical Methods

Analytical Methods utilized for medicinal plants are as follows;

2.1 Spectroscopic techniques

Extraction and segregation of solitary and multiple compounds from medicinal plants were conducted based on fundamental colorimetric determination, ultraviolet & visible (Hardy, 1938), and IR (infrared) spectroscopy. In quantitative applications, the analysis and chemical composition of glucoside in walnuts were examined (Daglish, 1950).

Several Spectrophotometric methods have been extensively utilized for the standardization and quantitative determination of a variety of biologically active compounds such as flavonoids, fundamental oils, phenolic compounds, and tannins) (Galvão et al. 2014; Grubesić et al. 2005; Aisha et al. 2013; Bokov 2018; da Silva et al. 2015; Alekandrovna et al.2019).

Essential nutrient elements were analyzed by the Indian researchers through AAS in a folk medicinal plant (Eucalyptus Oblique and Gava) (Santosh Teerthe 2018; Singh, et al. 1997).

Near-Infrared (NIR) spectroscopy is a reasonable and constructive analytical technique due to the addition of new computational software used in quality control analysis that differentiates the species. It provides quantitative information on metabolite content and isused in multivariate analysis. It also resolves the small contrast that occurs in metabolite content and also preserves sample integrity. Moreover, no sample preparation is required; as a result no need for solvents. It is a very good technique for discrimination of species and metabolites quantification. However, it is sensitive and only appropriate for sensing analytes greater than 0.1% (Fitzgerald et al. 2019). Wulandari et al. (2016) identified flavonoid content in medicinal plants by using UV- visible and NIR spectroscopy.

2.2 Chromatographic techniques

Paper chromatography is the classical technique that has been functional for the quality control analysis of medicinal plants (Paris and Viejo, 1955; Jaminet, et al. 1959; Hills and Rodwell, et al. 1951; Dybing et al., 1954; Krejci, 1958).

HPLC is a broadly used analytical technique, particularly in herbal products. Its components that performed the separation are entirely dependent upon discriminating attraction to the solid supports (stationary) and liquid (mobile) phases. It has been widely used in the analysis of the same compounds of complex mixtures. Due to its high-resolution technique, the conception of distinctive"fingerprints" has been build up for therapeutic plants and herbal-based products to support recognition and verification. Medicinal plant products, which are of the same type, from almost 40 separate manufacturers exhibited the differentiation under HPLC. Moreover, it also separates the nine marker chemical compounds (Fitzgerald et al., 2019). Numbers of research works have been published for the analysis of medicinal plants by the high-performance liquid chromatography, as few articles are summarized in the table below (Table 2).

Table 2. HPLC data of different compounds extracted from plants sources.

Compound	**Extract**	**Column**	**Mobile phase**	**Wavelength (nm)**	**Detector**	**Flow Rate mL/min**	**Ref.**
Flavonoids Biophenols & Phenols	*Olea europaea* L. (olives)	RP- C_{18} Bakerbond column (250 × 4.6 mm, 5 µm), connected with (50 × 4 mm) precolumn	**Solvent A:** Water:Acetic acid, (98 : 2) pH 3.1 **Solvent B:** methanol	230 & 278	Diode Array	1	Bianco, & Uccella, (2000)
Flavonoids (Antioxidants)	*Thymus vulgaris* L.	Alltima C_{18} RP, column (250 × 4.6 mm, 5 µm)	**Solvent A:** Water:Acetonitrile (3 : 1) acidified with glacial acetic acid (0.25%) **Solvent B:** Acetonitrile acidified with glacial acetic acid (0.25%)	210–450	Flourescence	0.85	Dapkevicius, et al. (2001)
Polyphenols (procyanidins)	*Vitis vinifera*	LiChrospher RP-C_{18} column (250 × 4 mm, 5 µm) connected with guard column (10 × 4 mm)	**Solvent A:** 1 L water +1mL85% H_3PO_4 **Solvent B:** methanol;	280	UV-Vis	1	Kennedy, et al. (2000)
Catechins & Epicatechins	*Crataegus*	LiChrosorb RP-18 column (250 × 4 mm, 5µm) connected with guard column (10 × 4 mm)	**Solvent A:** Methanol **Solvent B:** 0.5% *o*-phosphoric acid in water	280 & 220	-	1	Rohr, et al. (1999)
Isosteroidal alkaloids	*Fritillaria*	Nova-Pak C_{18} - RP column (150 × 3.9 mm, 4 µm)	Methanol containing 0.2% diethylamine,	224 nm	UV Detector	1	Lin, et al. (2001)
Coumarins (α-benzopyrones)	*Citrus aurantifolia*	Normal phase µPorasil (300 × 3.9 mm, 10 µm) column OR Nova-Pak C_{18} column (5 µm)	Ethyl acetate : hexane (1 : 4, v/v) OR **Solvent A:** Water:methanol (8 : 2, v/v), **Solvent B:** Water:acetonitrile (1 : 1, v/v)	335 and 310 nm	Fluorescence	1	Thompson, & Brown, (1984)
Coumarins	*Archangelica officinalis*	RP-18 column (250 × 4.6 mm, 5 µm)	Methanol:water with different ratio (8 : 2; 7 : 3; 6 : 4, v/v)	254	UV-Vis	1	Hawryl, et al. (2000)
Alkamides	*E. purpurea, E. pallida* and *E. angustifolia*	Hibar (125 × 4 mm, 5 µm) column, with LiChrospher 100 CH-18 LiChroCART precolumn (4 × 4 mm, 5 µm) with LiChrospher 100-CH;	Water: Acetonitrile Gradient elution from 40-80% within 30 min,	210 & 254	UV-Vis	1	Bauer, & Remiger, (1989)
Alkamides	*E. Pallida* (Asteraceae)	RP-C18, silica gel column (7.5 cm, 3 µm),	Acetonitrile:water (6 : 4, v/v)	210 & 260	UV detection	1	Binns, et al. (2001)
Polyacetylenes	*Cicuta virosa* L. (Apiaceae, Apioideae)	Spherisorb S5 ODS2 column (290 × 4 mm)	Methanol:Aqueous buffer 60-100%, Buffer (*o*-phosphoric acid 0.015 M, tetrabutylammonium	230	Diode array detector	1	Cimpan, & Gocan, (2002) ; Wittstock

			hydroxide 0.0015 M, pH=3)				, et al. (1995).
Miscelaneous	*Gastrodia elata Blume* (Orchidaceae)	ODS Zorbax SB-C_{18} column (250 × 4.5 mm, 5 μm)	Methanol:water:isopropyl alcohol (35:55:10, v/v),	270	-	0.4	Li, et al. (2001)
Soybean (seeds & roots)	Phytoalexins	**For RP-HPLC** Nova-Pak C_{18} column (150 × 3.9 mm, 4 μm)	**Solvent A:** Methanol; **Solvent B:** Aqueous buffer 0.01 M KH_2PO_4 (pH 2.4 with HCl) and 0.1% Et_3N (final pH about 2.46)	220	-	1	Faghihi, et al. (2001)
Soybean (seeds & roots)	Phytoalexins	**For NP-HPLC** Hypersil Si column (150 × 4.6 mm, 5 μm)	Hexane	254	-	0.8	Faghihi, et al. (2001)
Phytoestrogens	*H. lupulus* L.	Alltima RP C_{18} column (250 × 4.6 mm, 5 μm)	**Solvent A:** Formic acid in water **Solvent B:** Acetonitrile	280	-	0.9	Rong, et al. (2000)

This technique is an inexpensive and simple method in which a small amount of sample is needed without an advanced sample preparation method. Although it is a sensitive technique, it is best to detect contaminants. In performing HPTLC, thin layer chromatographic plates (as stationary phase) different solvent systems are required as a mobile phase. The sample was added by spraying it onto the plate, which then formed a band of the compound in a more reproducible and precise way. Moreover, the R_f factors (retention) of each compound are further testable (Fitzgerald et al., 2019). Senguttuvan and Subramaniam (2016) studied the methanolic extracts of leaf and roots of *Hypochaeris radicata* and thus validates its medicinal usage.

GC is utilized for the analytical determination of those compounds which are highly volatile. Previously, the methods that are employed for the compilation and manufacturing of these compounds werecompressing, steaming, and decontamination of herb-based materials. However, there are difficulties in introducing the sample into a gas stream, the intrinsic unsteadiness of volatile constituents, fatalities, and poor recovery of these substances. Therefore, microextraction techniques are beneficial for these techniques. Extraction techniques based on the needleare better because of their mechanization, simplicity of crossing point to further instruments furthermore, their compatibility with trimness (Steinmann, et al., 2011; Fitzgerald et al., 2019). Similarly, medicinal plant morphology and chemical composition of the volatile oil of various domestic species of china were successfully analyzed by the GC techniques (Zou, 2009).

2.3 Computational approaches

The number of computational approaches for the analysis of a variety of analytes takes part in the important function in computer-aided drug design (Jorgensen, 2004). Sharma and Sakar (Sharma & Sarkar, 2013) presented a quick and proficient method for the drug design and discovery of medicinal plants . Considering, computational drug discovery techniques Rallabandi et al., (2020) suggested that in future research should focus more on using computational biology to design new and more potent drugs for therapy with a better understanding of drug and receptor interaction.

2.4 Spray Drying Technique

Drying procedures are the most fundamental, quick, uncomplicated and universal methods that allow the rapid preservation of medicinal plant extracts and medicinal plant products like phytotherapeutics or phytomedicines and phytopharmaceuticals. In current era, many factors must taken into an account in order to apply drying methods such as level of production, quality standards of medicinal plant products and technology used. For inhibiting enzymatic activity, restrict microbial growth or increased shelf life by decreasing water content, drying technique also contributes in reduction of herbal plant volume with ease in transportation and storage.

Transformation of herbsbased raw materials into a medicinal product, appropriate for consumer andcurativefunctions, needs specialized operational processing and obviously complex in nature. Numerousmethods can be functional for this purpose,like freeze and spouted bed drying, fluidizedbed and spray drying.The most common ventilation or exposure to air technique used in the phytopharmaceuticalindustries for production of powdered medicinal plant products is spray drying that offers operationalelasticity, applicability for sensitiveto heatmaterials, in addition to an effective charge. Spray drying is a procedureby means of a liquid can convert into desiccated particles of micron size by a burning drying gasmedium. The spray-drying progressions diminish water activity of products, slow downthe microbial deprivationand broaden the product's shelf life (Vardin, and Yasar, 2012; Vladić, et al., 2016).

Chemical, physical and microbiological factors contribute to optimizing the spray drying procedurefor the stability of the medicinal herbs. These parameters depend on the humiditylevelof tissues at harvesting time, the plant components utilized, and the temperature most excellentapposite for conservation of the required constituents. This happened without compromising the quality parameter of generic constituents of medicinal plants. The rapid moisture reduction can be made by spray-drying via controlling humidity, flow rate, and temperature. The spray drying technique has been extensively utilized to acquireda larger concentration of biologically active ingredients in dry form.The literature overview of medicinal plants and their phytochemical activity is shown in Table 3.

Table 3. Medicinal plants and their phytochemical activities.

Medicinal plant	**Phytochemical activity**	**Literature survey**
Peppermint (Mentha piperita)	Antioxidant activity	Baranauskienė, et al. (2007)
Chamomile (Matricia chamomilla),	Prevent insomnia, antioxidanrt activity	Adib-Hajbaghery, et al. (2017).
Wild thyme or creeping thyme (Thymus serpyllum)	Antiobacterial activity	Shafique, et al. (2020).
Mountain germander (Teucrium montanum	Antioxidant activity	Vidović, et al. (2014).
Winter savory (Satureja montana),	Antioxidant activity	Vidović, et al.(2014).
Common yarrow (Achillea millefolium),	Antioxidant activity	Vladić, et al. (2016)
Common sage (Salvia officinalis),	Antioxidant activity	Alaşalvar, & Çam, (2019).
Lemon balm (Melissa officinalis),	Antioxidant activity	Tülek, et al.(2020).
Centaurea (Erythraea centaurium Pers.)	Anti inflammatory	Vidović, et al.(2014).
Rosmarinus officinalis (Rosemery)	Antispasmodic in renal colic and dysmenorrheal, in relieving respiratory disorders, choleretic, hepatoprotective and antitumerogenic activity, antioxidant activity	Souza, et al. (2008).
Marrubium vulgare	Antioxidant, anti-inflammatory and vasorelaxant effects, antimicrobial activity	Gavarić, et al.(2019).
Passiflora alata, and	Sedatives, hypnotics, tranquilizers, and anti-inflammatory, reduction of the hyperactivity in children,antispasmodics, and as pain relievers	Oliveira, et al. (2006).
Bauhinia forficata,	Hypoglycemic, depurative, and diuretic	Oliveira, et al. (2006).
Maytenus ilicifolia	Treatment of ulcers, indigestion, chronic gastritis, and dyspepsia	Oliveira, et al. (2006).
Bidens pilosa L.	Antimalaric, hepatoprotector, antimicrobial and antitumoral agent	Cortés-Rojas, et al. (2015).
Rhamnus purshiana (Cáscara sagrada) e	Natural laxative action	Gallo,et al. (2011).
Soyabean extract	Antioxidant activity	Georgetti, et al. (2008).
Eugenia dysenterica	Antioxidant activity	Couto,et al. (2011).

Morinda citrifolia L.	Antibiotic and antioxidant property	Krishnaiah,et al. (2012)
Orthosiphon stamineus	Antidiabetic , antiangiogenic and antiproliferative properties	Pang, et al. (2014)
Phyllanthus niruri e	Antimicrobial, anti inflammatory and analgesic properties	Gimbun,et al. (2018).
Curcumin extract	Antioxidant, antiseptic, antimicrobial and antitumoral substance	Araújo, et al. (2010
Orange peel	Antioxidant activity	Shofinita& Langrish (2014).
Murraya koenigii (Linn) curry leaves	Anti-oxidative, cytotoxic, antimicrobial, antibacterial, antifungal, anti-inflammatory, antiulcer, positive inotropic and anticholesterolemic activities	Sablania & Bosco (2018).
Averrhoa carambola pomace	Antioxidant activity	Saikia,et al. (2015)
Propolis extract	Antioxidant property	Marquele, et al. (2006)
Grapes	Cardioprotective effect, anti-cancer, anti-diabetes, antimicrobial, And anti-inflammatory properties	Kuck, et al. (2017).
Coffee	Antioxidant activity, antimicrobial activity, antidiabetic, anti inflammatory	Ballesteros, et al.(2017).
Saffron	Antioxidant activity	Khazaei,et al. (2014).
Acerola (Malpighia emarginata	Antioxidant activity	Rezende,et al. (2018).
Mint	Antioxidant activity	Sarkar, et al.(2013)
Flax seed	Antioxidant activity	Liu, et al. (2010).
Clove	Antiofungal, intiinflammatory and antibacterial activity	Chatterjee, & Bhattacharjee, (2013).
Coriander	Antimicrobial activity	Dima, et al. (2014).
Cinnamon	Antioxidant and antibacterial activity	Shahidi & Molaveisi, (2020)
Habanero chilli	Antioxidant and antibacterial activity	Domínguez-Cañedo, & Beristain-Guevara, (2011)
Psidium guajava L. (Yellow guava)	Antioxidant and antimicrobial activity, anti-viral, anti-inflammatory, anti-plaque and anti-mutagenic activities.	Mahfuzul Hoque, et al. (2007).
P. Boldus	Cholagogue, liver Stimulant	Gallo,et al.(2015).
R. Purshiana	Laxative for short-term Treatment of occasional Constipation	Gallo, et al.(2015).
C. Asiatica	Venotonic Anti-cellulite	Gallo,et al. (2015).
V. Officinalis M	Mild sedative and Sleep-promoting agent	Gallo,et al. (2015).
H. Virginiana	Venotonic for the Treatment varicose Veins	Gallo,et al. (2015).
H. Perforatum	Treatment of mild and Moderate depressive Episodes	Gallo, et al. (2015).
C. Scolymus	Adjunct treatment Of mild to moderate Hypercholesterolaemia, Antioxidant	Gallo,et al.(2015).

Pomegranate (*Punica Granatum* L.	Anti-atherogenic effects and anti-oxidative properties	Vardin, & Yasar, (2012).

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It is declared that there is no conflict of interest among the authors.

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