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Recent Advancements in Liquid Chromatographic Techniques to Estimate Pesticide Residues Found in Medicinal Plants around the Globe

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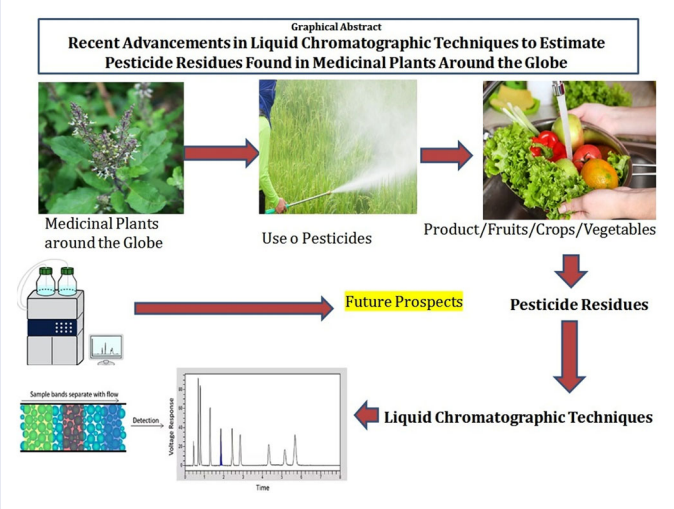
ABSTRACT

In the present review article, different advanced liquid chromatographic techniques and the advanced techniques other than liquid chromatography that are used to estimate the pesticide residues from different plant-based samples are presented. In the beginning of the article, details of pesticides, their health effects and various cell lines used for the related study has been outlined. Afterward, detailed descriptions regarding pesticides classification are inscribed. In the end, recent advancements in the area of analysis of pesticides for herbal drugs are explained. Solid phase micro extraction (SPME) and solid-phase extraction (SPE) are considered as most common method of sample preparation for pesticides and its residual analysis. The most commonly used analytical separation technique for pesticide analysis is liquid chromatography (LC) integrated with mass spectrometry (MS) and MS/MS as Triple Quadrupole Mass Spectrometer (QqQ) for the samples analysis where high level of sensitivity and accuracy is required in quantification.

KEYWORDS

ethno-medicinal research; insecticides; Liquid chromatography; multi-residue detections

GRAPHICAL ABSTRACT



Introduction

Almost all countries' healthcare systems have benefited tremendously by incorporating plant-based remedies. Plant parts used, plant-based preparations, and drug administration differs from place to place. However, knowledge of plant-based medicines is gradually fading, though some traditional herbal practitioners are still effectively practicing the art of herbal healing. These medicinal plants are frequently used by the area's residents to treat a variety of diseases. Research on ethnomedicine has uncovered a broad spectrum of possible sources for novel pharmaceuticals derived from medicinal plants.[1] Some modern medications have been developed from folklore and conventional medicine. Traditional societies have developed specialized knowledge about how to use wild plants and animals, much of which is unknown to those who live far from natural ecosystems like forests. This knowledge comes from living close to nature. The human community in general and healthcare professionals has identified useful and harmful members of the flora and fauna after years of observations, analysis,

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Figure 1. Balance of components.

trials, and errors. This demonstrates the fact that there is a positive relationship between the environment, medicinal plants, and human health.[2]

The triangular balance between the environment, medicinal plants, and human health as significant components is illustrated in Figure 1. Important bioactive medicinal compounds can be obtained in adequate quantities from medicinal plants. Also, the evolution of civilizations and the treatment of serious health problems—both are strongly affected by medicinal plants. For good health, many people depend on medicinal plants, which are fantastic source of medicine. The importance of using medicinal plants as a source of treatments or therapeutic aids has been known for years. The use of medicinal plants has transformed the global healthcare sector. This refers to the potential use of medicinal plants for both therapeutic and preventive reasons. Two thirds of individuals worldwide use herbal medicine as their main healthcare option.[3]

More than 50,000 plant species, or more than one-tenth of all plant species, are used in the manufacturing of pharmaceuticals and other health products. Having 11,146 and 7,500 species, respectively, China and India use the most medicinal plants. The percentage of medicinal plants ranges from Malaysia (7%) to India (44%, with Colombia, South Africa, the United States, and 16 other countries follow this.[4]

Certain plant families not only have a higher percentage of medicinal species, but also have high therapeutic potential. Around 12.5% of all species of plants currently in existence are employed as medicines. This percentage is changing on a daily basis as new research findings suggest that the medicinal value of these plants is increasing. Human health and the environment are also inextricably linked, as negative environmental change has a direct impact on human health. So, medicinal plants, human health, and the environment are all inextricably linked, and any factor that affects one will undoubtedly affect the other two. Hence, it has become important to provide information to general public, including healthcare professionals, with sufficient updates to promote a better understanding of the risks associated with the use of these plant based drugs and to ensure that all herbal drugs are safe and of acceptable quality.[5]

There is a possibility that medicinal plants may have a negative effect on health if pesticides and other such materials were used during cultivation. Consequently, it is crucial to quantify pesticide use and reduce its application whenever possible (Figure 2).[6]

The majority of losses associated with medicinal plants, whether in the field, during storage, or during pharmaceutical formulation manufacturing, are triggered by pests and harmful pathogens. Furthermore, the indiscriminate use of

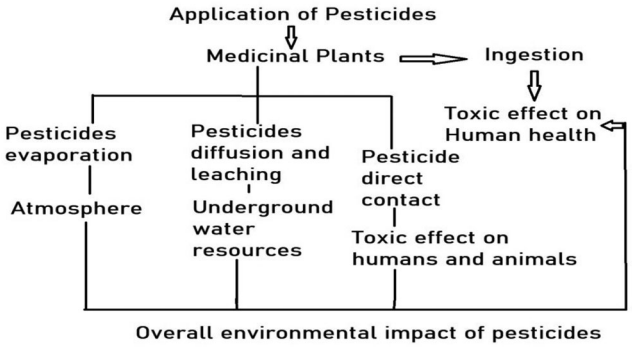

Figure 2. **Overall** environmental impact of pesticides.

synthetic pesticides has caused an array of problems, including insect resistance and contamination of essential world sources, such as plants, water, air, and soil.

So, pesticides originating from plants might be a greener option than synthetic pesticides to make crop production more efficient, reduce food shortages in a sustainable way, and keep people healthy. What matters is how we estimate pesticide levels in medicinal plants and what new developments have occurred in this area. Before putting medicinal plant-based medicines on the market, the amount of pesticides in each one should be estimated.[7]

There is no other way to keep medicinal plants pest-free other than to use pesticides on them. Pesticides are any chemical or combination of chemicals used to control, eradicate, or mitigate pests. Furthermore, pesticides termed as herbicide or weed-killers are employed to destroy undesirable plants while mostly sparing on the crop, we wish to grow and giving it nutrients. This makes the harvest of medicinal plants more profitable. Pesticide levels must be kept to a minimum in all conditions, and they must also be quantified on a regular basis. For periodic pesticide analysis of medicinal plants, robust, rapid, and reproducible analytical methods that can also detect minute pesticide concentrations are always required.[7]

For quantifying pesticide residues in medicinal plants, liquid chromatography, particularly HPLC, presents an array of reliable methods. The most prevalent HPLC method used nowadays is reversed-phase HPLC with a UV detector system. This is crucial for maintaining accepted pesticide levels below permitted limits for human consumption safe. One of the most crucial methods for preserving the aforementioned safe limits is HPLC. Nevertheless, it is frequently recommended to do sample cleaning and preparation before to HPLC testing. Usually, the nature of the sample dictates this. Aqueous samples normally suit liquid chromatography columns, although greater molecular weight matrices limit their versatility. Before analysis of chemicals with liquid chromatography, size exclusion chromatography (SEC) is commonly used to extract pesticides and purify both polar and non-polar chemicals.[8]

What are pesticides?

A category of synthetic or natural substances known as pesticides has been associated with environmental pollution as

Table 1. Details of pesticides, their health effects and various cell lines used for the related study.

S. no.	Pesticides and effective concentration	Health effects	Cell line used for the study	
1	Iprodione (10 μM) Chlorpyrifos (1 μM) Prochloraz (1 μM)	Dose-dependent Aryl hydrocarbon receptor (AhR) agonistic effects	Rat H4IIE and the Human TV101L hepatoma cell lines	[11]
2	Roundup Transorb® (67.7 μgL^{-1}) Furadan 350 SC® (0.1 μg L^{-1})	Can produce cytotoxicity when used in rice cultivation.	Zebrafish cell line, ZF-L	[12]
3	Fipronil (6.82 μM) Bupirimat (4.80 μM)	Androgen Receptor (AR) antagonistic activity.	MDA-kb2 reporter cell line	[13]
4	Methoxychlor (100 μM) Chlorpyrifos (100 μM)	Produce significant effects on gonadotropin-releasing hormone (GnRH) gene transcription and GnRH mRNA levels.	GT1-7 hypothalamic cell line	[14]
5	Herbicides (atrazine and glyphosate in concentration ranging 250 mg L^{-1}) Neonicotinoids (clothianidin, imidacloprid in concentration ranging 250 mg L^{-1})	Inhibit Retinoic Acid Catabolism.	Fish hepatic cell lines PLHC-1 and ZFL.	[15]

well as human health issues. Pesticides can enter the human body through medicinal plants, and since the COVID-19 pandemic, medicinal plants and herbal preparations have become commonplace for a large population.[9]

Since pests have become pesticide-resistant, crops should be protected with more synthetic pesticides yearly, which raises production costs and causes side effects. Pesticide-exposed foods and drugs raise the risk of cancers such non-Hodgkin lymphoma (NHL), leukemia, brain cancer, breast cancer, prostate cancer, lung cancer, stomach cancer, colorectal cancer, liver cancer, and urinary bladder cancer. To understand the health consequences related to pesticide exposures at the molecular level, cell culture is a good experimental model.[10] Table 1 represents the details of pesticides, their health effects and various cell lines used for the related study.

In addition to the use of personal protective equipment (PPE) that is effective in preventing harm to human health, users of pesticides must be cognizant of the risks associated to pesticides as well as how to appropriately manage it. Pesticide exposure has been associated to a number of illnesses, including those affecting the respiratory system, organs, and systems, as well as infertility, birth abnormalities, autism, ADHD, diabetes, and obesity. Cancer, birth deformities, teratogenic effects, neurological imbalances and developmental toxicity, immunotoxicity, and disturbances in endocrine function are still a few of the long-term, chronic negative consequences of exposure to pesticides.[16] By intake of pesticides in different forms or through dispersion into the medicinal plants, the use of pesticides has a detrimental effect on human health.

This is harmful to other animals and the environment. This renders assessing medicinal plant pesticide levels important. So, this review article summarizes advanced liquid chromatographic methods and other related cutting-edge liquid chromatography-based technologies utilized to quantify pesticides and pesticide residues.[17]

Even though a lot of work has been placed in analyzing pesticide residues in food and other specimens; it is being suggested that there is still a need for a good, repeatable analytical method for determining pesticides that may be employed on medicinal plants and pharmaceutical samples.[18]

Impact of pesticides on environment, human health and related consequence

Effective pesticides include insecticides, fungicides, herbicides, rodenticides, molluscicides, nematicides, and plant growth regulators (PGR). For instance, organochlorine insectides have been used successfully to combat diseases like malaria and typhus, but they are now prohibited in the majority of industrialized countries. Additional synthetic pesticides, including herbicides, fungicides and rodenticides e.g. organophosphates, carbamates, and pyrethroids are considered in pest management and boost agricultural productivity; but oral ingestion of high doses of pyrethroids may lead to complications in central nervous system symptoms including excitation and convulsions. Organophosphates and carbamates are absorbed through the gastrointestinal tract, lungs, and skin. They inhibit plasma and red blood cell (RBC) cholinesterase, preventing breakdown of acetylcholine, which then accumulates in synapses. Inhibition of cholinesterase causes acute muscarinic manifestations (e.g., salivation, lacrimation, urination, diarrhea, emesis, bronchorrhea, bronchospasm, bradycardia, miosis) and some nicotinic symptoms (e.g., muscle fasciculation). Carbamates are cleared from body within about 48 h after exposure but organophosphates, however, can irreversibly bind to cholinesterase and causes healthy problems. The PGRs in herbal medicinal products are seriously harmful impact on human health as they cause hepatotoxicity, nephrotoxicity, genotoxicity and even carcinogenicity and teratogenicity etc.

When considering about molluscicide (e.g. metaldehyde), it is used for controlling slugs and snails from lands where medicinal plants are grown but overdose application of this may result in severe muscle tremors, anxiety, hyperesthesia, ataxia, tachycardia, and hyperthermia. Another class of pesticides, namely, nematicides is a type of chemical pesticide that is used to kill nematodes (microscopic parasitic worms) that can live in soil, plants or water. Some nematicides, namely, Dibromo-chloropropane (1,2-dibromo-3-chloropropane), was used for over 20 years to control nematodes on crops, turf and in nurseries, but banned by the United States Environmental Protection Agency (US EPA) in 1977 because of clear evidences of infertility cases in men and induction of a variety of tumors in humans.

Even though crop output has been seen, Jayaraj et al. [19] stated that harmful effects have slowly started to show up. A pesticide should kill the insects this is meant to kill, but not other animals or people. Pesticides cause long-term and catastrophic sickness. Pesticides and other organic pollutants that stay around in agricultural soils without a purpose have had major environmental impacts.[20]

These insecticides are known to affect the normal functioning of the endocrine and reproductive systems of living organisms. Matisová and Hrouzková[21] remarked that many of these factors point out the significance of developing analytical chromatographic methods for precise pesticide analysis. A few researchers have linked certain pesticides, particularly dichlorodiphenyltrichloroethane (DDT), dieldrin, endrin, mirex, and hexachlorobenzene, to negative effects on human health and the environment. According to their application as herbicides, plant activators, growth regulators, molluscicides, insect attractants, insect repellents, and insecticides, pesticides are classified.[19]

Classification based on mode of action

Pesticides are classified into various categories based on how they work. The substances that fall under this category are contact pesticides, which kill pests *via* direct contact with the plant.[22] The skin is the route of entry for most pesticides. Such examples include Endosulfan, Malathion, and Fenvalerate[23].(Chemical structures are presented in supplementary file Fig. 1).

Pesticides acting on the basis of contact

Contact pesticides control pests when they come in direct contact with the pest. Weeds are killed when enough of their surface area is covered with a contactherbicide. Insects are controlled when sprayed directly, or when insects travelacross treated surfaces.

Stomach insecticides: These pesticides act within the digestive tract of their intended targets. Ingestion is the main route of entry for these compounds. Toxins produced by the bacterium *Bacillus thuringiensis* and rodenticides such as zinc phosphide (Zn_3P_2) are among the stomach toxins.[24]

Systemic insecticides: The active ingredients in these pesticides are absorbed by the roots as contact point and transported to other parts of the plant, such as the growth points, where they can influence plant-feeding pests. The xylem (the tissue responsible for transporting water) and the phloem (the tissue responsible for transporting nutrients) are two of the vascular tissues through which these pesticides disseminate systemically (food-conducting tissue). Insects which feed within the vascular plant tissues, such aphids, whiteflies, mealybugs, and soft scales, are particularly susceptible to systemic pesticides like Monocrotophos and Carbofuran (Chemical structures are presented in supplementary file Figure 1).[25]

Translaminar: These insecticides are absorbed by the leaf, forming a reservoir of pesticidal active ingredient therein. This provides long-lasting protection against pests that feed on plants. Translaminar insecticides and miticides include pyriproxyfen, chlorfenapyr (Pylon), and acephate (Orthene) (Chemical structures are presented in supplementary file Figure 1). These types of pesticides are generally effective against spider mites.

Fumigant: Fumigants, a type of gaseous pesticide, are used to get rid of unwanted pests in many different settings, including farms, homes, warehouses, and much more. As a rule, fumigants are extremely flammable and can penetrate deeply into a wide range of substances. Some of the most common fumigants are aluminum phosphate, methyl bromide, chloropicrin, and iodoform. Fumigants include DDVP (Dichlorvos), Lindane, and Chlorpyrifos (Supplementary File- Figure 1).

Classification based on chemical nature

The most popular and effective method for categorizing pesticides is based on both their chemical composition and the bioactive chemicals they contain. This type of grouping shows the efficacy of pesticides as well as their physical and chemical characteristics. Considering a pesticide's chemical and physical characteristics as it will assist in determining how to use it, what safety measures to take, and the amount to use, Pesticides are grouped into four main categories based on the ingredients they contain:

Organochlorine: Because of the multiple roles that organophosphate pesticides perform, these are categorized as broad-spectrum insecticides that are effective against a wide range of unwanted insects and animals. Differentiating factors include gastrointestinal poison, contact poison, and fumigant poison, all of which have the potential to cause nerve poisoning. Before a product can be sold, it has to first be evaluated. This is true regardless of whether the pesticides in question are biodegradable and might not have much of an effect on the entire environment. Organophosphorus insecticides are particularly dangerous to both vertebrates and invertebrates due to the fact that they inhibit the activity of the enzyme cholinesterase.

This causes a permanent layer of the neurotransmitter acetylcholine to cover a synapse. So, neuronal impulses can't move across the synapse. This causes voluntary muscles to twitch quickly, paralysis, and death.[20]

Organophosphorus: Pesticides containing organophosphorus (OP) include Malathion, Parathion, Diazinon, and others (Supplementary File- Figure 1). These are among the pesticides that are most frequently used. The most prevalent use for organophosphate pesticides is in application areas. These pesticides have a side chain that is composed of the chemically reactive phosphate ester and either two methoxy ($—OCH_3$) or ethoxy ($—OCH_3CH_3$) groups. Furthermore, they have a central phosphorous atom that is double-bonded to either an oxygen or sulfur atom.[26]

These pesticides inhibit acetylcholinesterase (AChE), which results in the development of toxic levels of acetylcholine in the nervous system. Similar to other esterase, butyl-cholinesterase can additionally be inhibited by

organophosphorus. The organophosphorylated enzyme is persistent, thus the patient's recovery from overdose may take some time, according to reports.[27]

Carbamates: Organophosphates and carbamates are similar compounds, but they come from different sources. Organophosphates are derived from phosphoric acid, whereas carbamates originate from carbamic acid. Carbamates can be synthesized from carbamic acid. Similar to organophosphate pesticides, carbamate pesticides work by interfering with nerve signal transmission, which increases poisoning and causes the pest's death. They are occasionally employed as fumigants, contact poisons, and stomach poisons. Under natural conditions, they are easily degraded with little environmental pollution. This group of insecticides includes some of the more popular ones, such as carbaryl, carbofuran, and propoxur, etc.[26] (Supplementary File- Figure 1).

Fipronil: Fipronil is an insecticide of to the phenyl pyrazole class that is used in veterinary ectoparasiticides. Fleas are typically killed on dogs and cats with the veterinary ectoparasiticide Fipronil TM. In the mid-1990s, fipronil, a phenyl pyrazole chemical, was synthesized as an effective insecticide. It is beneficial against the Colorado potato beetle and a few cotton pests that have adapted to conventional insecticides and are resistant to their activities. Fipronil is considerably less toxic to mammals than to insects.[29]

Pyrethroid: Pyrethroid insecticides are a distinct chemical class of active ingredients found in many new pesticides sold in stores, and pest control experts employ them. The term "pyrethroid" refers to the pyrethrum-like origin of this class of pesticides. In the 1990s, pyrethroids replaced previous insecticides, such as diazinon and Dursban®, and became popular as consumer insecticides. Some such pyrethroid pesticides may remain in the environment for a period of time, especially when protected from sunshine.

Others, including allethrin and resmethrin, degrade within minutes to hours after application. Acute pyrethroid poisoning rarely poses a risk of death, but large quantities of pyrethroid compounds can cause severe poisoning with a risk of death. Convulsions, coma, pulmonary edema, and hemorrhage are among the potentially fatal manifestations.[28] All of these studies indicate the need for liquid chromatography techniques and related developments for pesticide estimation.

Methodology for pesticidal analysis

The European Pharmacopeia (EP) approach for sample preparation is one of the most commonly used conventional procedures for assessing pesticide residues in medicinal plants, but it is also expensive, time-consuming, and requires large sample sizes and more harmful solvents. The development of quick, inexpensive, efficient, robust, and safe methods, such QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe), for routine application in laboratories is being encouraged by new trends in pesticide residue analysis which put an emphasis on simplified methods for preparing samples. Riedel et al.[18] in their research work has mentioned that this method is the best way to prepare samples for analysis by liquid chromatography coupled to mass spectrometry (LC/MS).The extraction efficiencies of the QuEChERS method were found to be far higher, and the sample preparation was much quicker. In most cases, the extraction efficiencies after the first step were approximately 100%.

The LC/MS techniques confirm the presence of pesticides in addition to providing qualitative and quantitative pesticide determinations. Because it requires the identification and quantification of hundreds of potential single chemicals, pesticide estimation is a daunting challenge. Despite the fact that medicinal herbs have a diverse variety of species, there haven't been many studies on the development of reliable standards for evaluating their quality. Some of the well-known and economically significant medicinal herbs cultivated and marketed in India are *Withania somnifera* (Ashwagandha), *Plantago ovata* (Isabgol), *Cassia angustifolia* (Senna), *Convolvulus prostrates* (Shankhapushpi), *Millettia pinnata* (Karanja), and *Andrographis paniculata* (Kalmegh).

As a result, a standard method for estimating pesticides from medicinal plants remains necessary. Consequently, the QuEChERS-based approach for identifying several pesticides in medicinal plants, including the fruits of *Malus pumila*, was modified, followed by LC-MS/MS analysis.[31]

In the 1960s and 1970s, thin layer chromatography was the most popular method for pesticide residue analysis. This was quickly abandoned with the advent of liquid chromatography (HPLC). The advantages of separation with HPLC compared to conventional methods include fast analysis times, and ability to analyze compounds with low stability.

Liquid chromatographic techniques used in estimation of pesticides in medicinal plants

In the niche area of chemical analysis known as pesticide estimation, liquid chromatography-mass spectrometry (LC-MS) is of vital importance. It is ideal to render a highly accurate and reliable determination that encompasses both qualitative and quantitative estimation of pesticide residues. Liquid chromatography (LC) coupled with tandem mass spectrometry (MS) is the preferred technique for the vast majority of pesticides because of the polar nature of the majority of pesticides currently in use, and especially of their metabolites. It is important to state that liquid chromatography-tandem mass spectrometry (LC-MS/MS) with triple quadrupole analyzer is highly appropriate for developing multiresidue methods of pesticide analysis, where up to 300–400 analytes can be simultaneously determined.[32]

These procedures will encounter difficulties because of the intricate nature of sample pretreatments, the requirement for highly trained professionals, and the expensive cost of equipment.[31] In comparison, rapid pesticidal analysis techniques, such as immunoassays, spectroscopic analysis, and electrochemical techniques, result in pesticide detection approaches that are relatively straightforward and

Table 2. Advanced liquid chromatographic techniques used for different sample/matrix.

S.No.	Analytical techniques	Sample/matrix	Other observed parameters	Ref.
1	HPLC-MS/MS Technique	Root of valerian, herbage of thyme, leaf of mint, root of common dandelion, leaf of lemon balm, herbage of common oregano;	Recovery 70–120%; Linearity $r^2 \geq 0.995$;	[36]
2	UPLC-MS/MS	Myristica fragrans (nutmeg).;*Thymus vulgaris*	Recovery 120%; Linearity $r^2 \geq 0.999$	[37, 38]
4	High-Performance Liquid Chromatography/Tandem Mass Spectrometry	Traditional Chinese Herbal Medicines (*Cortex cinnamomi*, *Flos carthami*, *Folium ginkgo*, *Herba pogostemonis*, *Radix ginseng*, and *Semen ginkgo)*	Recovery 70–110%; LOD < 0.01 mg/kg; Linearity $r^2 \geq 0.999$	[39]
5	LC–ESI-MS/MS (Liquid Chromatography- Electrospray Ionization- Mass Spectrometry)	Citrus fruits (Peel and pulp)	Recovery 95%; LOQ 5 μg/kg; Linearity $r^2 \geq$99%	[40]
6	HPLC	*Abelmosc hus esculentus L., Cucurbita Pepo, Solanum melongena L*	Recovery > 85%	[41]
7	LC-ESI-MS/MS	*Chamomilla recutita* and *Petroselinum crispum* (Dry herbs)	Recovery 70–120%; Linearity r2 ≥ 0.99; LOQ 0.01 mg/kg	[42]
8	LC-MS/MS analysis	*Ophiopogon japonicas* (Traditional Chinese Medicines)	Recovery 70-120%; Linearity $r^2 > 0.990$; LOQ 0.01 ng/mL	[43]
9	HPLC-QqQ-MS/MS	Rhodiola crenulata radix, Phyllanthus emblica (Ethnic medicines)	Recovery 70–110%; LOD 0.01 ng/mL; Linearity r2 >0.9987	[44]
10	liquid chromatography–tandem mass spectrometry)	*Panax ginseng, Serenoa repens*, and *Gingko biloba*	Linearity $r^2 >$ 0.99; LOD 0.09 ng/mL	[45]
12	UPLC–MS/MS	*Camellia sinensis* (Herbal Tea); Traditional Chinese herbal medicine;	LOD 0.5 μg/L; Linearity range 1.0–100.0 ng/mL	[46,47]
13	HPLC & LC-MS/MS	*Glycine max* and *Oryza sativa*	Recovery 94.3–102.6%; Linearity $r^2 > 0.9999$	[48]
14	HPLC	*Brassica oleracea* (Cauliflower); TriphalaChurna (Ayurvedic Medicine)	Recovery 87.7%; LOD 0.10 mg/kg; Linearity $r^2 > 0.9960$	[49,50]
15	LC-MS/MS	Ayurvedic Medicines and Dietary Supplements	Recovery 92.0%; Linearity range 2.5–500 ng/mL	[51]
16	LC–MS/MS	*Olea europaea* (Olive Oil)	Recovery 91%; LOD 0.01 μg/g	[52,53]

extremely sensitive.[33] Even if the accuracy and precision of these rapid methods are not as good as those of instrumental procedures, they can be used in conjunction with them, particularly as prescreening methods for locating objects in big samples.[34] Thus, there is a high demand for sophisticated analytical techniques for the fast and accurate determination of pesticides in medicinal plants and herbal drugs. Liquid chromatography (LC) is a versatile, dependable, and widely used method for isolating natural products. LC is a chromatographic method used to find, measure, and clean up the different parts of a mixture of phytochemicals.

LC is becoming more popular as the preferred method for fingerprinting studies to assess the quality of herbal drug samples. After a relatively crude extract is evaluated in a biological assay to fully characterize its properties, natural products are frequently isolated. For the high performance of multi-component samples comprising pesticides, the LC's resolving power is appropriate. Many secondary metabolites that are present in plant extracts, such as phenolics, steroids, flavonoids, alkaloids, and other pesticides, have also been classified and quantified by LC. Solntsev et al.[35] demonstrated that LC (HPLC, UPLC), and LC combined with other spectroscopy methods, including UPLC-MS/MS, may be used to quantify the amount of different types of pesticides in samples of medicinal plants. These methods provide a large variety of detector options, improving the accuracy of the analysis.

Currently, high-performance liquid chromatography (HPLC) and related techniques have become the dominant analytical separation tools in such areas as medicinal plants. Contrary to gas chromatography (GC), HPLC allows to determine low-volatile and thermolabile compounds. A variety of packing and bonded phases as well as eluents and their combinations make Liquid Chromatography technique very useful in analysis of medicinal plant contaminants, including pesticide residues. Unfortunately, besides advantages related to the use of pesticides, it should be taken into account that they are also toxic for humans and environment. As general population is exposed to pesticides mainly through the intake of medicinal plants and their parts, it is necessary to monitor concentrations of these compounds using sensitive techniques for ppm or even ppb levels. LC/MS/MS responds to the need for pesticide residue analysis resulting in methods that produce more reliable data to support medicinal plant safety monitoring programs. GC-MS is only preferred for less polar pesticides; for more polar compounds, LC-MS is more suitable. The need to deal with more polar pesticides as well as with pesticide metabolites, which are often more polar and less volatile than pesticide itself, is one of the main reasons for choosing LC-MS/MS over other similar techniques.

For the objective of identifying pesticides and pesticide residues in food, herbal remedies, and environmental materials, several researchers have developed LC methods[30] (Table 2).

High-performance liquid chromatography (HPLC) method

When it comes to analyzing a wide variety of samples, high-performance liquid chromatography (HPLC) is a reliable and accurate technique.[54] Separation in HPLC is achieved by distributing the sample analyte between a mobile phase (the eluent) and a stationary phase (the packing material of

the column). Depending on the analyte's chemical structure, the molecules slow down as they pass through the stationary phase. The amount of time spent "on column" is determined by the nature of the intermolecular interactions between the molecules in a sample and the packing material. This causes a variety of elution times for the various components of a sample. Therefore, researchers have to separate the components of the sample. Once the analytes have passed through the column, they are detected *via* detection methodologies. The signals are processed by a data management system (computer) and presented as a chromatogram.

After the mobile phase has passed through the detector unit, it can be sent to more detector units, a fraction collection unit, or the waste. In order to perform its function, a HPLC system requires a solvent reservoir, pump, injection valve, column, detector unit, and data processing unit. The pump forces the eluent through the system at a steady rate of pressure. If the researcher wants to keep the detector's signal as stable as possible and keep the noise level down, the pump's flow needs to be steady and pulse-free. The sample (analyte) is injected into the eluent through the injection valve.

The highest mycotoxin recovery from the *Oryza sativa* (rice) sample through the addition of NaCl was detected using high-performance liquid chromatography (HPLC). The salting-out effect on extraction efficiency was created by introducing 2% and 5% of NaCl in the dispersive liquid–liquid microextraction (DLLME) analysis.[55] Liu et al.[56] developed pesticide residue analysis using LC-QTOF/MS. It was found that the sample was cleaned up with primary and secondary amines, C18, graphitized carbon black, and anhydrous magnesium sulfate after undergoing an acetonitrile extraction step. For chili, the matrix effects were between −55.6% and 26.0%, and for Sichuan pepper, they were between −69.5 and 24.0%. The LOQ for all of the intended pesticides was less than 5 g/kg. After applying the procedure to real-world samples, researchers found pesticides at levels well above the maximum residue limit (MRL). The results confirmed the developed method's potential utility for quantitative pesticide analysis and non-target screening for potential metabolites in chili and Sichuan pepper samples.

UPLC-MS/MS

The chemistry method called UPLC-MS/MS combines the physical separation abilities of liquid chromatography with the mass analysis abilities of mass spectrometry. UPLC-MS/MS is a type of chemistry technique that combines the physical separation of liquid chromatography with the mass analysis of mass spectrometry. UPLC-MS/MS is a versatile technique with high sensitivity and selectivity. For the most part, it is employed for the detection and possible identification of chemicals in the presence of other chemicals (in a complex mixture) [57] . In order to get high-performance outcomes, the HPLC-based method is fused with sensitive mass spectrometric detection (LC-MS) and flexible tandem mass spectrometry (LC-MS-MS) in MRM mode. Known as liquid chromatography mass spectrometry and liquid chromatography mass spectrometry, respectively, this method is a dependable and widely accepted analytical tool for a variety of purposes, including the instantaneous, sensitive quantification and confirmation of a broad spectrum of target pesticides in complex matrices of drug samples. Ru-zhen et al.[58] developed an easy, and rapid method for carbamate pesticides in 2011.

Dispersive solid-phase extraction (DSPE), clean-up activities, and accelerated solvent extraction were used to remove carbamate pesticides from samples of *Radix glycyrrhizae* before analyzing them with ultra-performance liquid chromatography-mass spectrometry (ASE). Six different sorbent materials and four different extraction solvents were tested for their ability to remove interference from extracts. Three key analytical parameters, including extraction temperature, static extraction period, and static cycles, were also tested. This technique was utilized by Guo et al. (2012)[59] to determine the simultaneous concentrations of 15 pesticides in *Radix glycyrrhizae*. Traditional Chinese Medicine (TCM) is a system of healthcare that has been practiced in China for thousands of years and is based on the therapeutic use of plants.

Chen et al.[60] developed a fast multi-residue method for detecting 16 pesticides and pesticide metabolites from different classes in different types of TCM plants in just 15 m using modified QuEChERS extraction and UPLC-MS/MS analysis. The developed method for analyzing pesticides in TCM plants was easy, quick, and reliable. It produced high-quality results (good linearity, sensitivity, selectivity, recovery, repeatability, and analytical scope) and useful benefits (low cost, high sample throughput, little labor, almost no waste, and few labware and space needs). A rapid, efficient, simple, and high-throughput method for the simultaneous determination of 108 pesticide residues in three traditional Chinese medicines (TCMs) was established, comprising an improved QuEChERS method in combination with HPLC-MS/MS based on mixed samples. The method was also comprehensively validated and proved to be highly sensitive, precise, and accurate. It was also applied to the analysis of 60 batches of real samples. Pesticide residue analysis methods require simple and efficient pretreatment methods.[61]

There is a quick, simple, specific, and effective UHPLC-MS/MS method for instantaneous determination of pesticides in commonly consumed herbal products that was developed by Moreno-González et al.[62] Local markets in Granada, Spain, were shopped for the aforementioned chamomile, green tea, red tea, valerian, thyme, and linden samples. Many different types of herbal remedies were tested using the method, with encouraging outcomes. With UHPLC capabilities, separating pesticides could be done in just six minutes. The outcomes validated the method's viability for single-run pesticide monitoring in herbal products. Another once-ubiquitous herb, ginseng, is now so uncommon that it is used primarily as a traditional medicine in China. With its high medicinal value and positive health effects, ginseng and its processed products had captured a large fraction of the Chinese herbal medicine market,

properly accounting for more than 8% of overall total exports. When transporting medicines, pesticides are the main cause for alarm.

UPLC-PDA

UPLC is a miniaturized version of high-performance liquid chromatography (HPLC) that takes advantage of advances in technology in analytical performance, detector design, and data management. UPLC-PDA works on the principle of optimizing conventional HPLC by using columns with smaller sizes of particles (less than 2 m) that operate at a higher pressure, leading to substantial advancements in resolution, rate, and responsiveness. This new directive in analytical separation science[63,64] retains the ideas and utility of HPLC while improving analytical performance by a step function. UPLC is regarded as a novel technique that opens up new possibilities in liquid chromatography, especially in terms of reduced solvent consumption and analysis time. The UPLC system is built to withstand high system backpressure. Because of its up to 80% decline in mobile phase usage, shortened run time, and increased capacity, UPLC is regarded as a greener and more cost-effective substitute to conventional HPLC.[65] The distinct characteristics of UPLC enable it to conduct more complicated separation tasks while preserving analytical effectiveness.

UPLC-Q-TOF-MS

To quantify the number of pesticide species and metabolites, a pairing of LC and high-resolution mass spectrometry (e.g., quadrupole time-of-flight mass spectrometry) was employed. A recent paper described a prototype study focusing on the characterization of the formation of metabolites of the insecticide thiacloprid and the fungicides azoxystrobin and difenoconazole, as well as their analysis using liquid chromatography with high resolution mass spectrometry (LC-HRMS) methodology. 96 representative fruit and vegetable samples were selected for daily routine pesticide analysis and screened for pesticides as well as suspect pesticide metabolites.[66]

A multi-pesticide metabolite screening method utilizing liquid chromatography quadrupole time-of-flight mass spectrometry (UPLC-Q-Tof-MS) was created to identify the presence of pesticide metabolites in fruit and vegetable samples. Based on a retroactively created accurate mass compound database, a suspect was established by identifying pesticides of high concern that were developed and used on an extensive variety of plant-derived commodities. Ninety-six samples with positive detections for a total of 26 pesticides were re-analyzed in 100 samples from daily routine analysis for the appearance of corresponding metabolites. Forty-seven metabolites were identified using the UPLC-Q-Tof technique.[67]

In order to avoid any health complications originating from use of synthetic pesticides, the natural pesticides are recommended more. In this context, it is to mention that the roots of *A. pyrethrum* are used in traditional medicine of different countries to treat epilepsy, rheumatism, cephalalgia, paralysis and hemiplegia. *N-alkylamids* and ester pyrethrins are the main constituents of roots which have tremendous medicinal values. The plant is very good natural pesticide with considerable antimicrobial properties.[68,69] Additionally, innovative chemical and biological approaches are to be emphasized to control the pests.[70]

Matrix solid phase dispersion versus conventional (European Pharmacopeia) methods

As technology advances, the demand for accurate, rapid, and susceptible liquid chromatographic analytical methods for the analysis of medicinal plants and phytomedicines has increased. With the help of standardizing phytomedicines, these techniques are used to analyze the active plant compounds. Analytical studies aimed at ensuring the safe use of medicinal plants as well as their registration as phytomedicines are still lacking for the majority of them. So, research in the past has focused on making instrumental chromatographic techniques better so that they can be used in analytical procedures. High-performance liquid chromatography (HPLC), gas chromatography-mass spectrometry (GC-MS), liquid chromatography (LC), etc. have all been used to quantify pesticides by analyzing secondary metabolites, most notably terpenoids and flavonoids.[71]

Gingkolic acid, found in leaves extracts of *Gingko biloba* L. (Gingkoaceae), is an example of a potentially harmful plant substance that needs to be analyzed using sophisticated analytical methods in order to screen for their presence in phytomedicines.

Phytopharmaceuticals should also be examined for toxic substances, such as pesticide residues. Researchers in Brazil have been working in a methodical way to come up with new ways to measure pesticide residue.[72]

Through sample preparation innovations like SBSE (Stir Bar Sorption Extraction) and SFE (supercritical fluid extraction) (SBSE-HRGC and SFE-HRGC), these have been used to make fast methods that work with automated production lines. Pesticide residues have been detected in *Passiflora* L. plant species leaf infusions and other leaf samples used to make herbal medicine products utilizing this exact sample preparation.[73]

The efficiency of matrix solid-phase dispersion (MSPD) extraction was also compared to that of the EP referential method. One study used a student's t-test to compare the recovery and repeatability data of EP and MSPD for a few plant species. The MSPD method used fewer reagents and took less time to complete, and its efficiency in pesticide residues analysis was comparable to that of the EP method. This indicates that an MSPD-based procedure will produce accurate analytical results that could be compared to those of the reference EP method while having the advantages of being less complicated, quicker, and cheaper. The suggested method could be helpful as a screening protocol to help the herbal drug industry find pesticides in herbal medicines.

Table 3. Sample preparation methods for pesticidal analysis.

S.No.	Sample preparation method	Instrumental technique used for pesticides analysis	Ref.
1	Solvent extraction	HPLC-DAD	[75]
2	Ultrasonic extraction	Ion Exchange Liquid Chromatography	[76]
3	SPE	HPLC	[77]
4	Focused microwave-assisted extraction and solid phase extraction	SPME/HPLC/DAD	[78]
5	Soxhlet and microwave-assisted extractions	HPLC/Electron Capture Chromatography	[79]

Table 4. Comparison of advantage and disadvantage of LC techniques for Pesticide Analysis [80,81,82].

Name of liquid chromatography technique	Advantages	Disadvantages
HPLC	1. In HPLC, compounds are separated based on their affinity for either the stationary or mobile phase. This results in the compounds traveling through the column at different rates, leading to different retention times for each constituent. Improvements in technology are increasing the separation of the constituents whilst reducing the overall analysis time. 2. HPLC and MS can be hyphenated with each other. The mass spectrum of chemical entity separated by LC techniques molecule are generated using a mass spectrometer. The molecular mass and structure of sample components can be ascertained using this data. 3. Structural isomers that are difficult to separate using HPLC; in order to overcome this problem, it is to use a technique known as LC-MS/MS, where after ionization for MS, some of the ions are further fragmented. This allows the detection of structurally related isomers. HPLC allows to determine low-volatile and thermolabile compounds.	1. LC-MS is an expensive option, both in terms of capital and running costs. The ability to analyze a sample simultaneously for many compounds and the excellent data it can produce outweigh the high costs of its routine use. For e.g. HPLC can be a costly strategy because it requires countless costly organics and needs a force supply and ordinary support is required. 2. The instrument requires skilled personnel to set it up. However, after training, it is relatively easy to operate on a daily basis. 3. Structural isomers that are difficult to separate using HPLC can also be difficult to detect with MS. The ions generated for use in MS from structural isomers can be too similar to show differences in m/z ratios.

The quality of the samples used for quantitative and qualitative analyses of pesticides and their residues is very important, as the latter value data shows.[74] The work done by several researchers in the field of sample preparation for pesticidal analysis is presented in Table 3. The composition of medicinal plants is much complicated and, in this context, sample pretreatment techniques, especially solid-phase extraction (SPE), liquid-phase extraction (LPE) and supercritical fluid extraction (SFE) are indispensable which could eliminate the interfering substances in the sample matrix, enrich analytes to present to the detectable level of analytical equipment, namely, LC-MS/MS, obtain the detection results with highest level of accuracy. This in turn, enhances the specificity of pesticide residue detection.

Apart from this, recently, biosensors are getting great attentions and it is known for unique applications in the detection of pesticide residues which could covert the specific target recognition into the recognizable signals for e.g. optical signal, or electrical signals etc. On the basis of these signals, pesticides can be detected from complex plant sample also.

Recent advancements in the area of analysis of pesticides for herbal drugs

In addition to the existing liquid chromatographic method, there are numerous estimation methods for pesticides, including ELISA, etc. Each method of pesticide analysis has advantages and disadvantages. High level of recovery and reliability in quantification of pesticides are the most important advantages of using LC, but the expensive running and cost of purchasing, repairing, and maintaining the instruments, as well as the increased analysis time of each sample, are the major disadvantages of liquid chromatography method.

These are presented in Table 4.

Techniques utilizing antibodies for the quick detection of multiple residues

Rapid detection methods for pesticides have relied on the use of antibodies as their primary recognition element for some time now. As an alternative to conventional methods for detecting pesticides in food and environmental samples, antibody-based methods such as the enzyme-linked immunosorbent assay (ELISA) have been used. Several methods exist to obtain broadly specific antibodies for pesticide residue analysis, as mentioned by Jia et al.[34]

Generic antibodies are produced by immunogens with a "general structure," and they are one type of broadly specific antibody. Broad-spectrum antibodies are yet another type of broadly specific antibody, and they can be made by immunizing a mouse with multiple haptens simultaneously. Bispecific antibodies, which have two distinct heavy and light chains, have been extensively used as broadly specific antibodies since the advent of genetic manipulation and hybridoma technology. Finally, multiple analyte-specific antibodies can be combined to recognize multiple targets and produce a broadly specific antibody.[34]

Pesticide detection in environmental samples can be accomplished using a variety of techniques based on immunochemical reactions. The ELISA technique employs antibodies in conjunction with enzymatic markers. This approach is currently the most popular and preferred one. Competitive ELISA is used for pesticide and residue analysis[83] due to the low molecular weight of pesticides. An

Table 5. Techniques employed for different types of samples analysis.

S. no.	Technique	Sample/matrix	Reference
1	Enzyme-linked immunosorbent assays	Food, herbs and environmental samples	[85]
2	Gas Chromatography	Crops, plants, foods and environmental matrices.	[86]
3	Ion chromatography	Herbal drugs, foods and environmental matrices.	[87]
4	Capillary electrophoresis	Crops, foods and environmental matrices.	[88]

indirect competitive ELISA (IC-ELISA) was created in a recent study by using a monoclonal antibody with high affinity for five antibacterial synergists. Also on the rise is the use of the IC-ELISA method. With this antibody, a direct competitive ELISA (DC-ELISA) method was developed in place of the more laborious and time-consuming enzyme-labelled secondary antibody IC-ELISA. But the DC-ELISA method is considered a fast and low-cost approach to pesticide analysis in food, drugs, and environmental samples. The chemiluminescence enzyme-linked immunosorbent assay (ELISA) was developed to increase the sensitivity of the aforementioned technique.[84] In order to determine the concentration of pesticides in medicinal plants and other environmental samples, scientists use a variety of analytical methods, some of which are detailed in Table 5.

Surface-enhanced Raman scattering (SERS) based Multi-Residue detections

SERS is a well-liked technique that uses nanotechnology and Raman spectroscopy together for the early screening of pesticide samples from plants. The chemical bonds and vibrational properties of functional groups can be seen in the Raman spectral bands. This gives a fingerprint for the analyte of interest. SERS can be used to find and measure analytes with good accuracy down to the level of a single molecule because of the effect of SERS substrates. In order to improve SERS sensitivity, a number of pesticides that modify surface properties have been created. Because of advances in SERS substrates, multi-residue detection in a complex matrix is now the method of choice for analyzing crucial pesticide samples.[59] Apart from Surface Enhanced Raman Spectroscopy (SERS) with advantages of rapidness; high sensitivity and ability of field-test has been considered as a powerful emerging tool for the analysis of pesticide residues from complex samples.

Recent advancements in area of liquid chromatography method for pesticides estimation

When multiple matrices interfere with one another, the procedure for detecting pesticides in real samples becomes murky. Recently, gas chromatography have replaced by other advanced liquid chromatography methods for detecting and quantifying pesticides in various matrixes including medicinal plants, fruits and vegetables etc. as the most popular options, attributable to their selectivity, dispersion ability, and ease of identification.[86]

Table 6 shows some recent work done by researchers in the area of liquid chromatography methods for qualitative and quantitative estimation of pesticides, as well as their other details.

Recent study conducted on quantification and risk assessments of pesticides in herbal medicines using LC/MS-MS and other techniques has suggested that presence of pesticides has been observed in the majority (88%) of a comprehensive cross-section ($n = 1771$) sample. The observed pesticides concentration was beyond the limit a mentioned in European Pharmacopeia (EP). The studies suggest for the application of herbal medicine quality-control measures using HPLC technique to ensure the safeguard against potentially serious health risk posed to the majority of the global population consuming herbal medicines having pesticide content.[88]

Overuse of pesticides has been identified as an important concern in herbal remedies. When focusing the latest technologies and trends in the area of pesticide detection from plant-based samples etc, Aptamer- and Molecularly Imprinted Polymer (MIP)-based biosensors have received greater attention in recent years. However, there are just a few aptamers at present that target pesticides because of the challenges in selecting small molecules from complicated sample of plants etc. There is currently no appropriate receptor for the development of biosensors in view of same. The field of aptamers must turn its interest from selecting unmodified aptamers to producing modified aptamers, which would broaden the range of strong interaction for aptamers. Modified aptamers are currently utilized primarily in the fields of therapeutic strategies and biomedical fields, but the lack of straightforward, affordable selection methods for these continues to be a major bottleneck. Larger targets like proteins and complete cells present substantial hurdles for MIPs because there aren't many water-soluble functional monomers accessible, and these targets still showed considerable nonspecific binding and can't access their respective recognition sites because of their size.[89] Other than these advancements, some optical methods for estimation of pesticides has been also used and still advanced version is in process of search which includes electrochemiluminescence, photoluminescence, phosphorescence, competitive fluorescence-linked immunosorbent assays (cFLISA), enzyme-linked immunosorbent assay (ELISA), lateral flow immunoassay (LFIA) and high fundamental frequency quartz crystal microbalance (HFF-QCM) etc.[90.] These in turn suggests the most appropriateness of Liquid Chromatography method for pesticide estimation.

Future trends in pesticides analysis

It has been elucidated that utilization of reversed-phase high-performance liquid chromatography (RP-HPLC) followed by UV diode array detection is most advantageous

Table 6. Recent work done by researchers in the area of liquid chromatography method for qualitative and quantitative estimation of pesticides.

S.No.	Work Done	
1	A QuEChERS modified method was used for pesticide residue determination from several key medicinal herbs. LC–MS/MS analysis was employed for this.	[91]
2	Liquid chromatography separation, and tandem mass spectrometry, which enabled determination of 82 pesticides from important medicinal plant cannabis	[92]
3	Using high-performance liquid chromatography coupled with tandem mass spectrometry, Hou et al.[93] developed a novel analysis method that enabled for the simultaneous determination of 31 pesticides in ginseng.	[93]
4	Using ultrahigh-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry, Chen et al.[60] performed a simultaneous analysis of 40 different pesticide residues that were detected in tobacco.	[94]
5	A method for the simultaneous determination of pesticide adjuvants in medicinal plants derived products was developed. 2-Pyrrolidone, *N*-methyl-2-pyrrolidone, and *N*-ethyl-2-pyrrolidone were quantified. The technique was based on an isotope-labelled internal standard. LC–MS/MS was combined with a modified QuEChERS extraction method.	[95]
6	A sensitive and cost-effective method for the quantitative analysis of azole pesticides residues in six medicinal plants was established based on magnetic cyclodextrin cross linked with tetrafluoroterephthalonitrile (Fe_3O_4@TFN-CDPs) coupled with high-performance liquid chromatography (HPLC). Magnetic cyclodextrin polymers were synthesized and used as an adsorbent for this study.	[96]
7	Cebi et al.[97] used liquid chromatography-tandem mass spectrometry to analyze pesticide residues in hazelnuts using the QuEChERS method.The hazelnut (also known as the filbert), is a type of nut that comes from the medicinal plant *Corylus avellana* which is mostly cultivated in Turkey, Italy, Spain and the United States.	[97]
8	Coconut tree (*Cocos nucifera L.)* is an economic tree, food and oil source ubiquitously distributed in several countries in different regions globally. Oils are used for medicinal purposes too. Pesticide levels of imported and local samples of coconut oil were determined using HPLC following standard procedures.	[98]
9	A new reliable, fast and highly sensitive method based on ultra-high performance liquid chromatography tandem mass spectrometry has been developed and validated for the determination of 28 carbamates in aromatic herbs. The combination of QuEChERS with UHPLC-MS/MS introduces a high-throughput methodology for the monitoring of these residues in this type of matrices scarcely explored.	[99]
10	To improve productivity and control pesticide residues; three different methods of extraction for pesticides were applied and methods based on chromatographic separation HPLC with mass spectrometric detection(LC-MS/MS tandem spectroscopy) considered useful methods for determination of pesticide residues in products based on medicinal plants etc.	[100]
11	*Cannabis sativa* L. as important medicinal plant extracts have quickly become popular products due to their health-promoting effects. However, potential contaminants, such as mycotoxins and pesticides, can be coextracted during the manufacturing process and placed into the final product.Using ultra-high-performance liquid chromatography coupled with quadrupole Orbitrap high-resolution mass spectrometry (UHPLC-Q-Orbitrap HRMS), Narváez et al., 2020, developed a novel methodology for quantifying 16 mycotoxins produced by major *C. sativa* fungi. This has been followed by a post-target screening of 283 pesticides using an extensive spectral library.	[101]

and accurate method. Prior to LC analysis, a SPE is to be used to estimate the analytes concentration and to perform the process of sample clean-up. Specificity, selectivity, linearity, precision, accuracy and limit of quantification (LOQ) are considered as important validation parameters of liquid chromatography when used for estimation of pesticides from medicinal plants samples. In order to meet future requirement, attempts are being made to simplify the analytical procedures and to make cost effective, quick and accurate method along with advancements in Instruments for analysis .

The two most frequently employed sample preparation methods for analysis naming, SPE and solid-phase microextraction (SPME), have been modified with the aim of greater recoveries and no emulsion problems. In terms of advancement in this area, system of LC is commonly combined with MS and MS/MS due to their exceptionally sensitive detection as well as quantification. The pattern of pesticide analysis has indeed been dramatically changed with significant innovations in liquid chromatography.

Future analytical method development must enable for the rapid, precise, low-cost, and simple analysis of pesticides. LC–MS is rapidly becoming a routine technique for the efficient trace analysis of polar pesticides in various types of samples. In comparison to existing methodologies LC–MS considerably simplifies clean up procedures, reducing both time of analysis and method development time The time-consuming sample preparation and lengthy run time of the GC-MS technique delay the result, which is essential to the identification of pesticides in specimen. LC-MS/MS is the favored method for analysis due to its higher sensitivity, smaller sample volume requirement, improved LOD/LOQ, a quicker clean-up and simple preparation of samples procedure, and decrease run time. Liquid-liquid extraction (LLE) applying organic solvents for LC-MS/MS analysis of pesticide samples offers sample cleaning and analyte enrichment steps, and is a robust off-line sample preparation method that is suitable for routine high-throughput LC-MS/MS analysis. Based on previous research performed by various scientists, it has been established that the LC-MS/MS method requires less sample volume, fewer reagents, and less analytical time, resulting in lower sample preparation costs. With regard to sample preparation, the LC-MS/MS method requires only two simple steps, whereas the GC-MS method requires several steps, including SPE and derivatization with a more critical chemical, as trimethyl sulfonium (TMSH) etc. This resulted in a significant decrease in total analysis time. It is pertinent to point out that sample preparation prior to injection for GC-MS is approximately ten times more time-consuming than for LC-MS/MS.

LC systems have also improved in user-friendliness and integration with the MS, and sample clean-up has begun to be integrated into various LC front-ends. It is now conceivable that in the near future we will have integration of liquid handling, sample extraction/clean up and LC with each other in a single MS-front-end, which in turn will be highly integrated with the MS/MS instrumentation, with all being interfaced bi-directionally to a Laboratory Information System.

It can be highlighted that hyphenated liquid chromatographic methods are preferable and possess still scope of development in future for more accurate, quick, and cost-effective pesticide and pesticide residue analysis. Based upon the data presented and highlighting the contemporary

research as presented, future research can shape their research in a good way using this review article as reference.

Conclusion

The assessment of pesticide residues from herbs and herbal product has great importance to consumer health protection; and the development or usage of robust and economical analytical methods is highly required. Various studies involving HPLC, LC-MS/MS, GC-MS/MS, Ion Chromatography, TLC, Capillary electrophoresis etc. have been conducted to address this issue. The majority of pesticide residue analysis equipment and methods used today require numerous organic solvents, expensive sample volumes, prolonged analysis timeframes, and large sample sizes etc. The LC-MS/MS techniques are best suited for pesticide estimation from herbs. Further, it is concluded that hyphenated analytical techniques needs to be explored more for getting higher degree of automation and higher sample throughput. Liquid -Liquid Extraction is preferred choice for pesticide sample extraction at present. The present review article showcases the new, relatively simple and reliable analytical methods for qualitative and quantitative determination of pesticide residues in medicinal plants. The analytical efficacies of the liquid chromatography for different medicinal plants are highlighted and additionally, we end by touching on the future prospects for the contemporary cutting-edge sophisticated analytical liquid chromatography-based technologies for pesticides analysis.

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