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A Brief Review of Recent Advances in Surface-Enhanced Raman Spectroscopy and Microfluidics Technology for the Ultrasensitive Detection of Pesticides

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Abstract

The pesticide is any substance used to prohibit, destroy, or control pests, such as insects, fungus, rodents or, undesirable plant species that cause damage during crop production and storage.

There are a lot of traditional methods to detect pesticides, among them gas chromatography (GC), high-performance liquid chromatography (HPLC), and their combinations with ultraviolet (UV) or mass spectroscopy. Nevertheless, these conventional techniques have several limitations, involving complicated pre-treatment steps, requiring expensive instruments, operational difficulty, lack of instrument portability, and difficulties in real-time monitoring.

Surface-enhanced Raman spectroscopy (SERS) is one of the current leading techniques widely applied for the ultrasensitive detection of pesticides molecules. SERS takes advantage to combine the high specificity of Raman scattering with the signal amplification of electromagnetic enhancement provided by the excitation of surface Plasmon resonances in metallic nanostructures, together with the charge transfer mechanisms established between metal surfaces and analytes.

In this brief review, types of classification of pesticides that can be classed have been reported. These classifications can provide valuable information on the chemistry of pesticides. The state of art of SERS, including a theoretical background study, is briefly described. Finally, some recent development and applications of optical and analytical techniques for pesticides detection have been summarized; a particular study will be focused on SERS combined with microfluidic technology that has appeared as advanced tools for surface enhanced Raman spectroscopy (SERS). They have been demonstrated to be interesting for in situ and real-time detection of analytes at extremely low concentrations.

Keywords: SERS; microfluidic technology; Raman soectroscopy; detection of pesticide.

1.Introduction

The pesticide is any substance used to prohibit, destroy, or control pests, such as insects, fungi, rodents, or undesirable plant species that cause damage during crop production and storage [1]. A pesticide is generally a chemical or biological agent (such as a virus, bacterium, or disinfectant) designed to kill or retard the growth of pests that damage or interfere with the development of crops, shrubs, trees, wood, and any other vegetation desired by humans.

Targeted pests may include insects, plant pathogens, weeds, mollusks, nematodes (roundworms), and microbes that cause nuisances, spread disease, or are vectors of disease. Despite the social benefits of pesticide use, there are many disadvantages, such as potential toxicity to humans and other animals [2]. Pesticides can be classified in many ways; these classifications can provide valuable

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information on the chemistry of pesticides, how they work, what they target, etc [3]. Pesticide detection is an essential part of regulating and monitoring pesticide levels in the environment. Although GC/LC-MS is often the reference method for pesticide detection, recent technological advances have enabled the development of alternative techniques, such as enhanced surface Raman spectroscopy (ESRS), which offers additional features such as highly sensitive detection, faster turnover, simpler protocols, in situ sampling, on-site capacity and reduced cost [4]. However, the consistency and repeatability of SERS-based techniques is a challenge due to the complexity of detection environments. This disadvantage can be overcome by integrating SERS detection into a microfluidic platform, which can provide a continuous flow condition for highly reproducible SERS measurements. In addition, the SERS microfluidic platform can perform elaborate sample pretreatments, which has great potential for on-site analysis of food contaminants [5]. In the first part, the principles of Raman spectroscopy will be presented starting with a description of the delivery mechanism. Then we will expose the exalted Raman effects of resonance and surface, the latter originating from chemical and electromagnetic mechanisms. We will also see The SERS-microfluidic system as a microfluidic analysis platform in which the SERS technique performs the function of detection. The second part mainly summarizes the classification of pesticides. The synthetic pesticide is classified into organochlorines (OC), organophosphates (OP), carbamate, synthetic pyrethroids which are commonly used because of their advantages in plant cultivation.The third and final chapter, we have discussed modern detection methods over the last three years for each group of pesticides, in particular, the Surface Enhanced Raman Spectroscopy (SERS) technique, a label-free detection method capable of providing high sensitivity, offering remarkable possibilities for analytical applications in fast and simple protocols and relatively inexpensive experiments.

2. Background

2.1. Raman spectroscopy

Raman scattering is a physical phenomenon, experimentally demonstrated in 1928 by the Indian physicist Chandrasekhara Venkata Raman during the study of light scattering by liquids. Although the experimental discovery was made by C.V. Raman, who was awarded a Nobel Prize in 1930, the phenomenon had been theoretically envisaged as early as 1922 and 1923 by L. Brillouin and A. Smekal respectively. Raman spectroscopy is a non-destructive chemical analyzing technique that gives details on chemical structure, crystallinity, phase and polymorphism, and molecular interactions. It is based on the interaction of light with chemical bonds within a material [6]. When monochromatic radiation is incident on a sample, this light interacts with the sample in one way or another. It can be reflected, absorbed, or scattered in one way or another. The scattering of the radiation from the molecule or material provides information about the molecular structure of the samples. The analysis of the overall scattered radiation with the same wavelength than the exciting radiation (Rayleigh scattering) but also a weak radiation that is scattered at a different wavelength (Anti-Stokes and Stokes Raman scattering). (About 1 x 10^{-7} only of the scattered light is Raman). It is the variation in the wavelength of the scattered photon that gives the chemical and structural information [7].

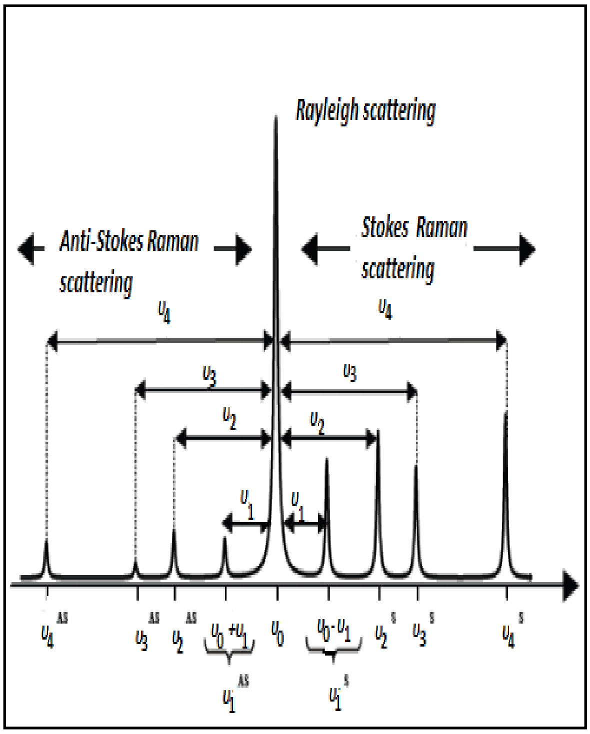

Fig. 1. Schematic representation of a Raman spectrum.

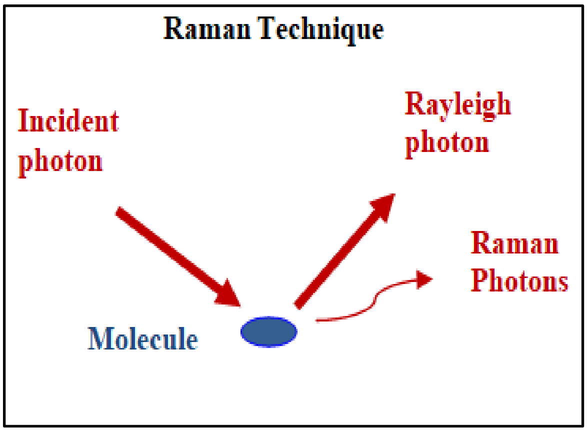

Fig. 2. Schematic diagram of the Raman technique.

2.2. Surface Enhanced Raman Spectroscopy (SERS)

In case of very low concentration and low intensity, Raman signals can limit the use of Raman technology. In this case, we use SERS which uses the same illumination and detection system as the one used for the normal Raman system, the only difference is due to the metallic substrate mainly (Au, Ag, and Cu) to exalt the intensity of the Raman response of the molecules [8].

Surface-enhanced Raman scattering (SERS) was discovered in the seventies of last century by the Fleischmann group who observed a surprisingly strong Raman signal of a single monolayer of pyridine on an electrochemically roughened silver electrode. The experiment was soon confirmed and quantified by the Van Duyne group and Creighton group, reporting that enhancement of RS of pyridine is in order of 10^5 –10^6. Surface-Enhanced Raman Scattering Spectroscopy (SERS) is focused on the considerable improvement of the Raman scattering of molecules adsorbed on suitable metal nanostructures (mainly gold and silver)[9]. Valuable information regarding the preparation of AuNPs and AgNPs is obtained from the procedure described by Jana Kubackova et al. [10] due to the difficulty of detecting small concentrations of molecules of great interest to the environment, spectroscopic techniques are used to detect traces of pesticides at low dosages, notably SERS scattering is one of the most powerful non-destructive analytical and diagnostic techniques employed [11]. Two kind of mechanisms are contributory to the total improvement: the charge-transfer (or molecular) mechanism that implies an increases the polarisability of the molecule, and the electromagnetic mechanism that is based on the enhancement of the electric field on the metal surface promoted by the resonance excitation of surface Plasmon-polaritons in metal nanoparticles [9]. By the electromagnetic mechanism, the incident light induces the collective oscillations of the electrons of the conduction band of a noble metal (gold or silver), this oscillation creates plasmon waves. In nanoparticles, plasmon wave takes a different form; we speak of localized surface plasmon (LSP)[12].

(LSP) depends on the shape of the nanoparticle (nanostar, triangular nanorods, nanoprisms...), the size of the nanoparticles(NP) must be smaller than the wavelength of an electromagnetic wave[13], and its dielectric environment (optical index n) and the polarization of the light (important because it can excite several plasmons) [14]. And as a result of this oscillation, a strong increase of the electromagnetic field is generated closer to the metal surface. Charge transfer theory involves the hybridization of the molecular orbital of an analyte molecule with an orbital from the metal surface. The largest enhancement is observed when the energy of photons of the incident light is tuned to the difference between the energy of the Fermi level in metal and non-occupied orbital in the analyte molecule or is tuned to the difference between the energy of the highest occupied orbital in the analyte molecule and the Fermi level in metal. The total averaged enhancement factor in surface-enhanced Raman scattering measurements can be considered as the combination of both effects leading to average enhancement ratios of about 10^4 to 10^6, but values in the order of 10^{11} can even be achieved in some cases. As a result of such an enormous enhancement factor, it is possible to record SERS spectra from very diluted samples, and it is even possible to record a reliable spectrum from a single molecule [15].

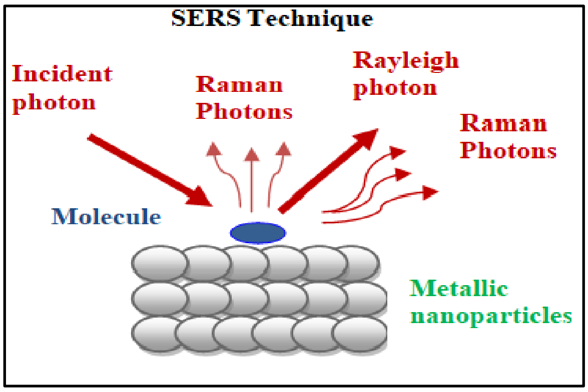

Fig. 3. Schematic diagram of the SERS effect.

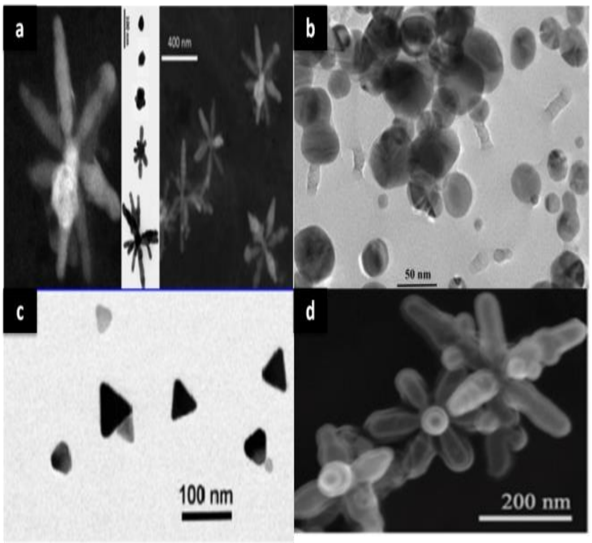

Fig. 4. Selected examples of nanoparticle shape and size. a) Star-shaped morphology of AgNPs observed in the TEM image, adapted from Ref [16], used with permission; b) spherical silver nanoparticles observed in the TEM image, adapted from Ref [17], used with permission; c) Nanoprism silver nanoparticles observed in the TEM image, adapted from Ref [18], used with permission; d) Au/Ag hollow nanostar, adapted from Ref [19], used with permission.

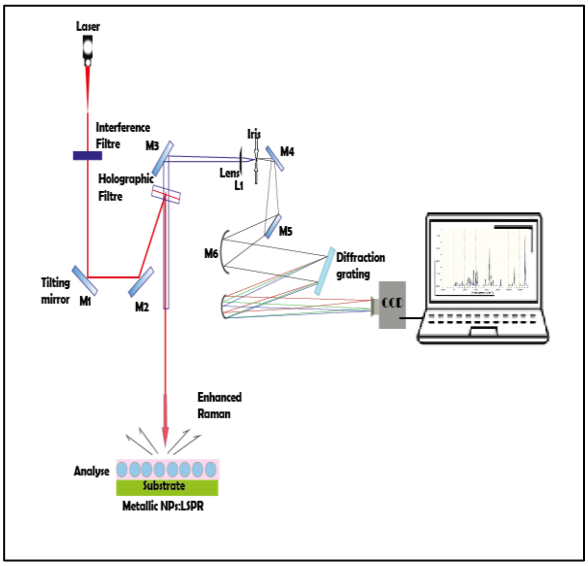

Fig. 4. Experimental setup for the SERS measurements.

2.3. SERS-microfluidic system

Microfluidic, also called “micro Total Analysis System (mTAS)” or “Lab on a Chip (LoC)”, integrates all necessary analytical techniques, including sample-preprocessing and final detection, into a chip. This method is aimed at manipulating a small number of fluids in channels with width/depth dimensions of micrometers. In comparison to conventional macroscopic instruments, Microfluidic systems have many benefits, such as low dosage, reliable process control, high performance, and portability. A representative microfluidic chip is mainly composed of a micropump, a micromixer, a microvalve, and a detector. The detector is an essential part of microfluidic devices. In contrast to the conventional fluidic platform, the small sample volumes often encountered in microfluidic devices represent a huge challenge for the detectors. Thus, the detection mechanism achieved by means of microfluidic further increases the sensitivity and specificity to the target analyte. Early in the development of microfluidic detection, off-chip detection methods such as MS or HPLC were widely used in a microfluidic platform. However, off-chip detection methods do not allow continuous monitoring of the target analytes of a large batch of samples because the samples must be removed from the chip reservoir at each detection. Currently, other studies are focusing on on-chip detection technologies such as electrochemical and optical methods. The most widely used technologies are optical detection techniques, which mainly include ultraviolet-visible spectroscopy (UV-Vis), fluorescence spectroscopy, Fourier transform infrared spectroscopy (FTIR), and SERS. Among these methods, SERS is emerging as a superior technique featuring label-free fingerprint Raman spectra of analytes with narrow spectroscopic bands as well as ultra-high sensitivity. In addition, SERS can provide analyte information very quickly, with measured latencies in the order of seconds or even fractions of seconds, enabling real-time monitoring processes. The SERS-microfluidic system can be defined as a microfluidic analysis platform in which the SERS technique performs the detection function [4]. And as a result, the interest of microfluidics is to control the flow and mixing of solutions (colloidal solution and solutions to be analyzed) and thus optimize the amplification of Raman scattering of molecules at a very low concentration underflow[20].

In one of the branches of the T-channel, we inject the silver colloid solution, and in the second branch, the solution contains the molecules of known concentration. The mixing of the nanoparticles with the molecules being done by diffusion, a diffusion zone is created in the center of the channel where the Raman scattering signal of the molecules is exalted by the silver nanoparticles. At different points of the channel, and at different distances Y from the mixing zone, there is a meeting point of the two fluids and for each meeting point, there is a mixing time that corresponds to each distance. When the mixing time increases the intensity also increases. As a result, we will notice that the amplification of the Raman signal has increased[21].

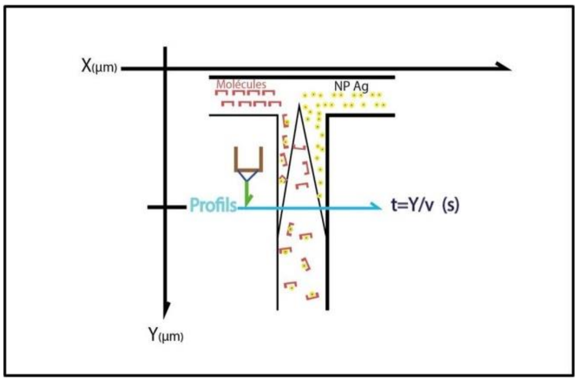

Fig. 5. Microchannel of T shape.

3. Classification of pesticides

The word "pesticide" is a general term for all insecticides, herbicides, fungicides, rodenticides, wood preservatives, garden chemicals, and household disinfectants that can be used to kill certain pests. Because pesticides vary in identity, physical and chemical properties, synthetic pesticides are classified based in different ways according to need. However, there are three most popular ways of classifying pesticides, which are; classification based on the (i) mode of action, (ii) targeted pest species, and (iii) chemical composition of the pesticide [22].

3.1. Classification based on the mode of action

Pesticides are classified according to how they act to achieve the desired effect in this classification. In this type of classification, pesticides are classified as non-systemic and systemic pesticides. Non-systemic pesticides are those that do not significantly penetrate plant tissues and are consequently not transported within the plant vascular system. On the contrary, systemic pesticides are those that effectively penetrate plant tissues and are transported within the plant vascular system to bring about the desired effect [23].

3.2. Classification based on the targeted pest species

Classification by target pests is probably the most popular. For example, insecticides are pesticides that target insects, and herbicides target plants [7]. The others are rodenticides to control rodents, fungicides to control fungi, wood preservatives to protect the wood, virucides to control viruses, bactericides to control bacteria, garden chemicals, household disinfectants, etc.

3.3. Classification based on the chemical composition

In this type of classification, pesticides are distinguished by their chemical nature and active ingredients. This classification is considered the most useful one for researchers studying the field of pesticides and the environment because it gives a more accurate idea of the efficacy and physical and chemical properties of pesticides. In addition, and the structure also provides information about the specific prevention that needed during the application rates [24]. Depending on chemical properties, pesticides are classified into four main groups, namely; organochlorines, organophosphorus, carbamates, and pyrethroids.

Organochlorine pesticides (also called chlorinated hydrocarbons) are organic compounds bonded to five or more than five chlorine atoms. They represent one of the first classes of pesticides ever developed and are applied in agriculture. Most of them are generally applied as insecticides for the control of a wide range of insects and have a long-term residual impact on the environment. These insecticides can impair the proper function of the nervous system of the insects leading to disorders such as convulsions and paralysis, followed by probable death. Common examples of these pesticides include DDT, lindane, endosulfan, aldrin, dieldrin, heptachlor, toxaphene, and chlordane**.** despite the production and usage of DDT has been banned in most developed countries, including the United States, many years ago it is still produced and being used in most tropical developing countries for disease vector control [1].

Organophosphorus are phosphoric acid-derived pesticides, considered one of the broad-spectrum pesticides consisting of a heterogeneous group of chemicals, which control a wide range of pests, weeds, or plant diseases because of their multiple functions. These pesticides are most effective for use against vertebrates and invertebrates because OPs include cholinesterase inhibitors that will cause a permanent overlay of acetylcholine neurotransmitter via a synapse [25]. As a result, nerve impulses do not move across the synapse causing a rapid contracting of voluntary muscles, hence, leading to paralysis, which is associated with death. Some of the widely used organophosphorus insecticides include parathion, malathion, dichlorvos, diazinon.

Carbamates are a type of insecticides structurally and mechanistically equivalent to organophosphate (OPs) insecticides. Carbamates are N-methyl

Carbamates derived from a carbamic acid and cause carbamylation of acetylcholinesterase at neuromuscular junctions and neuronal synapses. Although they have a working mechanism similar to the irreversible phosphorylation of acetylcholinesterase by organophosphates, carbamates attach reversibly to acetylcholinesterase. Afterward, carbamates have a toxicological presentation that is similar to that of OP intoxications with a toxicity duration generally less than 24 hours [26]. Widely used insecticides this group include carbaryl, carbofuran, and aminocarb [22].

Pyrethroids are chemicals that kill insects, in particular mosquitoes. They can be an important factor in helping to stop the spreading of the West Nile virus. Mosquito control professionals mix pyrethroids with oil or water and put it as a very low-volume spray that kills flying adult mosquitoes. When used correctly, pyrethroids present very little risk to human health and the environment [27] . The commonly used synthetic-pyrethroid pesticides are cypermethrin, fenvalerate, fluvalinate, pyrethrin, and permethrin [1].

4. Detection of pesticides

There are a lot of traditional methods to detect pesticides, among them gas chromatography(GC) [28], high-performance liquid chromatography (HPLC) [29] , and their combinations with ultraviolet (UV) or mass spectroscopy, are widely used for the detection of pesticides residue in agricultural products. Nevertheless, these conventional techniques have several limitations, involving complicated pre-treatment steps, requiring expensive instruments, operational difficulty, lack of instrument portability, and difficulties in real-time monitoring. Despite immunoassays [30], electrochemical methods [26], and capillary electrophoresis [31] are common rapid detection techniques, they also suffer from some inherent flaws, like instability of the solution and limited stocking time [32]. Surface-enhanced Raman spectroscopy (SERS) is an emerging detection technology, based on label-free detection method capable of providing high sensitivity, offering remarkable possibilities for analytical applications in fast and simple protocols and relatively inexpensive experiments [33].

5. Analytical methods

*5.1. Detection of organochlorine pesticides***:** So far, several analytical tools have been employed for detecting OPs substances. The most common methods are gas chromatography coupled with electron capture detection (ECD), electrolytic conductivity detector, or mass spectrometry. Gas Chromatography (GC) has also been used with Fourier transform infrared spectroscopy (FTIR). These methods are used to determine aldrin, dieldrin, and α- and β-endosulfan in water, air, municipal effluents, sludge, and soil, in human body liquids, fish, food, and feces. The detection of lindane is yet imperfectly identified, but there is a method available to determine lindane and its metabolites in urine, serum, and feces samples utilizing HPLC-UV-Vis. Although there are some advantages to these analytical methods, such as velocity and sensitivity of detection, all of these methods require sample preparation and are quite expensive. Thus, SERS should be used as an easy, fast, sensitive, non-destructive, and inexpensive method to detect these pesticides [2].

5.1.1. Dichlorodiphényltrichloroéthane (DDT) was one of the more important pesticides that were widely used in agriculture, forestry, and public health, particularly from the mid-1940s to the mid-1960s. The application of DDT and other chlorinated pesticides resulted in the contamination of the human food chain with this compound and its metabolites [68]. In 2018,(Al-Saleh et al.) conducted a study on DDT in aquatic fauna by gas-chromatograph coupled with an electron capture detector (GC-ECD). The risk to human health from exposure to DDT through fish consumption was investigated. This study revealed surprisingly high levels of OCPs that pose a high risk and are above international acceptable levels. National authorities should therefore consider reducing the potential risk of these pollutants to human and wildlife health [34]. In the same year, (Lili Niu et al.) conducted a study on the presence of DDT in the soil and air samples. In this study, DDT concentrations in the soil and air samples were quantified by gas chromatography (GC) with a mass spectrometer. Total DDT concentrations in soils were observed to be higher, indicating a higher potential risk to ecosystems. The existing and potential carcinogenic risks of soil DDTs were higher, while those of air DDTs were lower. The results of this study can provide a comprehensive understanding and scientific basis for managing and avoiding ecological and human health risks [35].

Table 1: Detection techniques for the analysis of pesticides

Detection method	Pesticide	Class of pesticide	Reference
GC-ECD	Dichlorodiphényltrichloroéthane(DDT)	Organochlorine pesticide	[34]
GC-MS	Dichlorodiphényltrichloroéthane(DDT)	Organochlorine pesticide	[35]
HPLC	DDT and carbaryl	Organochlorine pesticides	[36]
SERS	α-endosulfan, β- endosulfan, DDT , aldrin, and heptachlor	Organochlorine pesticides	[37]
XRD and XPS	Endosulfan	Organochlorine pesticide	[38]
GC-HRMS	α- and β-endosulfans	Organochlorine pesticides	[39]
LC-HRMS	Endosulfan	Organochlorine pesticide	[40]
SERS	Methyl-parathion and parathion	Organophosphorus pesticides	[41]
QB-ICA	Parathion	Organophosphorus pesticide	[42]
MPH-TG Biosensor	Methyl –parathion	Organophosphorus pesticide	[43]
MIP sensor	Malathion	Organophosphorus pesticide	[44]
FRET-based up-conversion fluorescence sensor	Malathion	Organophosphorus pesticide	[45]
UHPLC-MS/MS	Malathion	Organophosphorus pesticide	[46]
μ-SPE –FT-IR spectroscopy	Diazinon	Organophosphorus pesticide	[47]
LC-MS/MS	Diazinon	Organophosphorus pesticide	[48]
HPLC-DAD	Diazinon	Organophosphorus pesticide	[49]
SERS	Carbaryl	Carbamate pesticide	[50]
HPLC	Carbaryl	Carbamate pesticide	[51]
UPLC–MS/MS	Carbaryl	Carbamate pesticide	[52]
SERS	Carbofuran	Carbamate pesticide	[53]
UV- spectrophotometric	Carbofuran	Carbamate pesticide	[54]
Electrochemical non-enzymatic sensor	Carbofuran	Carbamate pesticide	[55]
UV/Vis spectrophotometer	Cypermethrin	Pyrethroid pesticide	[56]
DLLME-HPLC with ultraviolet detection	Cypermethrin	Pyrethroid pesticide	[57]
VSLLME-HPLC	Fenvalerate	Pyrethroid pesticide	[58]
HPLC	Pyrethrins	Pyrethroid pesticide	[59]
GC-MS	Pyrethrins	Pyrethroid pesticide	[60]
Gas-liquid chromatography	Fluvalinate	Pyrethroid pesticide	[61]

GC-ECD: Gas chromatography-electron capture detection; GC-MS: Gas chromatography-mass spectrometry; HPLC: High-performance liquid chromatography; SERS: Surface-enhanced raman spectroscopy; XRD and XPS: X-ray diffraction and x-ray photoelectron spectroscopy;GC-HRMS: Gas chromatpgraphy-high resolution mass spectroscopy;LC-HRMS: Liquid chromatography-high resolution mass spectroscopy; QB-ICA: Quantum dots-immunochromatographic assay; MPH-TG Biosensor: Methyl parathion hydrolase fused with glutathione-S- transferase; MIP sensor: Molecular imprinted polymer sensor; FRET-based up-conversion fluorescence sensor: Fluorescence resonance energy transfer-based up-conversion fluorescence sensor; UHPLC-MS/MS: Ultra-performance liquid chromatography-tandem mass spectrometry;μ-SPE-FT-IR spectroscopy: Micro-solid phase extraction-fourier transform infrared spectroscopy; DAD: Diode array detection; UV/Vis: Ultraviolet/visible; DLLME:Dispersive liquid-liquid microextraction;VSLLME:vortex-assisted surfactant-enhanced emulsification liquid-liquid microextraction.

Table 2: Summary of pesticides, class of pesticide, nanosubstrates used

Pesticide	Class of pesticide	Substrate	Reference
α-endosulfan, β- endosulfan, DDT , aldrin, and heptachlor	Organochlorine pesticides	AgNPs/ SERS	[37]
Methyl-parathion and parathion	Organophosphorus pesticides	AuNPs/ SERS	[41]
Carbaryl	Carbamate pesticide	AgNPs/ SERS	[50]
Carbofuran	Carbamate pesticide	AuNPs/ SERS	[53]
Fipronil	Organophosphorus pesticides	AgNPs/ SERS	[62]
Deltamethrin	Pyrethroid pesticide	Au@Ag NPs/SERS	[63]
Imazalil	Organochlorine pesticides	AgNPs/ SERS	[33]
Dipyridinic derivatives	Carbamate pesticide	AuNPs/ SERS	[64]
Paraoxon-methy	Organophosphorous pesticide	AuNPs/ SERS within a microfluidic channel	[65]
Thiabendazole, thiram, endosulfan, and malathion	Organophosphorous pesticide, carbamate pesticide, organochlorine pesticide, organophosphorous pesticide	Au@Ag NPs/SERS within a microfluidic channel	[66]
Thiram	Carbamate pesticide	Au@Ag NPs/SERS coupled with paper-based microfluidics	[67]

Also, other studies have also been conducted to detect DDT. Lourdes Cervera-Chiner et al. analyzed DDT and carbaryl pesticides in honey using immunosensors.In recent years, the presence of pesticides in honey has raised concerns because residues of DDT and carbaryl have been found in honey samples. Among the available techniques, such as high-performance liquid chromatography (HPLC), but are not suitable because of their high cost and the need for highly qualified staff. Immunosensors are becoming an interesting alternative to classical immunoassays for pesticide detection as they offer the advantages of real-time output, sensitivity, simplicity, and cost-effectiveness [36]. De Zhang et al. also conducted a study of the prepared "Bridge" substance solution to detect organochlorine pesticide, was obtained Raman spectra of the bridge substance and the pesticides molecules by utilizing DFT with the hybrid B3LYP functional based on the Gaussian 09 computational package. and for obtaining the SERS spectra of the "bridge" substance was added organochlorine pesticide solution(DDT,....) into the "Bridge" solution followed by stirring for 5 min. After that, a little of the prepared solution was withdrawn with a pipette and put in the cylindrical quartz. Then starting the scan to obtain the SERS spectra. The result was compared the SERS spectra of "bridge with the results calculated by DFT, DDT can be easily identified by the peaks .some other frequently used organochlorine pesticides were also detected by this "bridge" technology based on SERS [37].

5.1.2. Endosulfan is a cyclodiene insecticide that exhibits a fairly wide spectrum activity. Endosulfan is a combination of two stereoisomers, α, and β-endosulfan. It is widely used worldwide to control insect pests in a wide range of crops and, most importantly, it has been used for the control of Helicoverpa sp. in the cultivation of cotton. This insecticide has been used widely for more than 30 years on a variety of vegetables, fruits, cereals, and cotton as well as on trees, vines, and ornamental plants. Endosulfan is highly toxic to fish and other aquatic organisms and impacts the central nervous system, liver, kidney, blood, and parathyroid gland; it has reproductive, teratogenic, and mutagenic effects. Endosulfan (α- and β endosulfan) once introduced into the environment is transformed to endosulfan sulfate in the soil and remains as a significant residue. Endosulfan sulfate is the only degradation product considered toxic [69]. Tauqeer Abbas et al.

conducted a study on endosulfan-contaminated surface and groundwater in South Africa. Therefore, endosulfan must be removed from the water to minimize human health risks. Adsorption on activated carbon [70], membrane filtration [71], and photocatalytic techniques [72], were used to remove endosulfan in water. iron-containing composites have also demonstrated their potential to breakdown a number of chlorinated contaminants. waste from the iron industry known as "iron turning waste" is used as a filtration medium to remove endosulfan in water. Iron turning waste was characterized using X-ray diffraction (XRD) and X-ray photoelectron spectroscopy (XPS) before and after its reaction with endosulfan. Batch studies showed that it efficiently removed endosulfan in water even when the contamination level was 100 times higher than the USEPA drinking water standards [38]. In 2020, (Leesun Kim et al.) conducted a study about the levels and distribution patterns of α- and β-endosulfan and endosulfan sulfate in air, water, soil, and sediment samples in South Korean. Gas chromatography was coupled with a high-resolution mass spectrometer (GC-HRMS) was used for the analysis of endosulfan. The results of this study indicate that endosulfan present in environmental media is mainly from agricultural areas although the prohibition of its production and use. Endosulfan sulfate, a metabolite of α- and β-endosulfans, was the prevalent form of endosulfan in all of the environmental compartments monitored in this study. Thus, it is essential to continuously monitor endosulfan in all environmental compartments to control its illegal use [39]. Hwa-Kyung Lee et al. performed the metabolism of endosulfan sulfate in human liver preparations (human liver microsomes, S9 fractions, and hepatocytes) to detect new metabolites using liquid chromatography-high resolution mass spectrometry (LC-HRMS). Endosulfan sulfate is a primary oxidized metabolite of the organochlorine insecticide endosulfan. using LC-HRMS, Six metabolites were identified, including 5 novel metabolites of endosulfan sulfate. These results are not similar to the metabolic pathway of endosulfan and suggest the possible detoxification metabolic reaction of endosulfan sulfate in living organisms [40].

5.2. Detection of Organophosphorus pesticides: Several analytical techniques have been employed so far for detecting OPPs substances. The most common methods: gas chromatography-mass spectrometry (GC–MS), liquid chromatography-mass spectrometry, capillary electrophoresis, pressurized liquid extraction), and fluorimetry and liquid-solid extraction (LSE), GC and LC are frequently used. The mentioned chromatographic methods have been combined with mass spectrometry, such as LC-MS and GC–MS [73]. These methods have their own limitations such as difficulties in real-time monitoring, operational complexity, and lack of instrument portability. Thus, it is needed to develop methods for in situ, rapid, sensitive, and non-destructive detection of pesticides. Recently, several non-destructive techniques such as spectroscopy, computer vision, hyperspectral imaging, and Raman chemical imaging have been developed for food quality and safety evaluation. Among them, spectroscopic techniques have attracted much attention because of their fast response time and ease of use. In particular, Raman spectroscopy, especially surface-enhanced Raman spectroscopy (SERS) is a powerful technique for direct and rapid detection of pesticides due to its non-destructive nature, high sensitivity, no interference with water, narrow spectroscopic fingerprint, and very easy sample preparation [74].

5.2.1. Methyl-parathion and parathion are closely linked, non-systemic contact organophosphate pesticides that are active against aphids, capsids, leaf miners, sawflies, and weevils. They differ only by the substitution of a methyl or ethyl group on the phosphate ester. Methyl parathion is widely used in fruit (e.g. oranges, apples, and grapes), vegetables (e.g. string beans), and rice; parathion is still used in several developing countries. Because of its greater toxicity to humans and greater persistence, the ethyl form (parathion) has been linked to cases of pesticide poisoning, leading to the decline or cessation of its use in many countries [75]. Jie Xie et al. conducted a study on the paper-based SERS substrate for the rapid detection of methyl parathion on the surface of apple fruit. First, the paper-based substrate was manufactured. In addition, the SERS performance of the paper-based substrate was detected. Next, a sample (the peel of the apple) spiked with methyl parathion was sampled to check the practicality of the substrate by a simple (paste-peel off) method. Afterward, the SERS spectrum was recorded. In the conclusion, we can say the method based on the SERS substrate is inexpensive and can be used for on-site inspection. Most importantly, its preparation process is relatively simple. The test of methyl parathion in the actual sample has made the feasibility of this method in analytical fields, especially in environmental issues and food safety [41]. Also, (Beibei Liu et al.) developed an immunochromatographic assay (QB-ICA) to assess on-site parathion in farm produce. Three types were sampled of agricultural product vegetable, apple, and rice were spiked and analyzed via QB-ICA for method validation. In recent years, nanotechnology has developed rapidly, especially in terms of semiconductor materials, triggering the flowering of many types of fluorescent semiconductor nanocrystals; they are also commonly referred to as quantum dots (QDs) and have been used as an ideal candidate indicator in the ICA format. Quantum dot submicrobeads (QBs), which are polymer matrix embedded with numerous QDs, exhibit a stronger fluorescent intensity than the corresponding QDs, resulting in higher analytical sensitivity compared to QDs used as probes in the ICA. However, there are only a handful of studies of QB-ICA for the detection of pesticides [42]. Witsanu Senbua et al. fabricated a simple and effective absorbance-based biosensor using recombinant methyl parathion hydrolase fused with glutathione-S-transferase (MPH-GST) biosensor for the identification of the pesticide methyl parathion. In this study, the concentration of MP was detected in the water sample and in some agricultural products (i.e., grapes, tomatoes, basil leaves, Chinese kale, coriander, red peppers, yard-long beans, Chinese cabbages, watermelons, asparagus). The use of the MPH-TG Biosensor compared to GC-MS analysis showed that the percentage of MP recovery obtained with the MPH-TG Biosensor was very close to that obtained with GC-MS analysis. The results indicated that the proposed absorbance-based MPH-GST biosensor could be used effectively for such detection with high accuracy [43].

*5.2.2.Malathion:*Malathion (dimethoxyphosphinothioyl butanedioate) is a broad-spectrum, non-systemic organophosphorus pesticide widely used to control insect pests on crops, gardens, and household products. The human population may be exposed to malathion from residues in food, drinking water,malathion-containing personal use products, residential areas where malathion is sprayed, and during pesticide application. Malathion may cause diminished acetylcholinesterase activity, oxidative stress, hepatotoxicity, metabolic disturbance, neurotoxicity, cytotoxicity, immunotoxicity, and genotoxicity in target and non-target species [76]. Youssra Aghoutane et al. conducted a study of a sensitive and selective molecular imprinted polymer (MIP) for the identification of MAL in olive oils and fruits based on the screen-print gold electrodes (AuSPE). Using acrylamide as the functional monomer the MIP sensor was prepared and MAL as the template. Furthermore, the morphology of the electrode surface was studied, by scanning electron microscopy (SEM) and atomic force microscopy (AFM). The electrochemical characterization of the developed MIP sensor was performed by differential pulse voltammetry (DPV), cyclic voltammetry (CV), and electrochemical impedance spectroscopy (EIS) techniques. The developed method has shown to be rapid, highly accurate, and inexpensive for quantifying low levels of MAL residues in contaminated olive oil and fruit samples. This paves the way for the use of this sensor to detect low levels of MAL residues in foodstuffs and other environmental matrixes. the obtained results provide new opportunities to detect other OPPs contaminants in various food products as well as in soils, tap waters, and waste [44]. Quansheng Chen et al. used a FRET-based up-conversion fluorescence sensor in foods to detecting malathion in adulterated matcha samples and tap water with high precision. a highly sensitive fluorescent aptamer sensor was evolved for the determination of malathion, the system was premised on a cationic polymer-mediated fluorescence ‘turn-off’. Malathion-specific aptamers were related to the cationic polymer through electrostatic interactions. To produce fluorescence resonance energy transfer (FRET), negatively charged upconversion fluorescent nanoparticles (UCNPs) and cationic-polymer encapsulated gold nanoparticles (GNPs) were joined together. This combination resulted in fluorescence quenching, and the degree of quenching was related to the concentration of malathion. It appears by the results recorded that the sensor has a strong potential for malathion assay in real samples [45]. In 2020, (Mohamed Habila et al.) conducted a study about the microextraction procedures were followed by the determination of malathion by ultra-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). The aim of this work was to optimize and develop dispersive solid-phase microextraction procedures to isolate malathion from water and food samples using copper-benzyl tricarboxylic acid-based metal-organic frameworks (Cu-BTC-MOFs) as adsorbent. In this study, was detected the concentration of MAL into the Tap water sample and also, some foods (i.e., Apple, tomatoes, Mango, Green onion, Cucumbers, Beans). The results that were obtained for fruits, water, and vegetable samples indicate the high performance of the Dispersive solid-phase microextraction (DSPME) procedure for malathion analysis [46].

5.2.3. Diazinon: Diazinon (O, O-diethyl O-[6-methyl-2-(1-methylethyl)-4- pyrimidinyl] phosphorothioate) is an organo-phosphorus insecticide classified by the World Health Organization (WHO) as "moderately hazardous" belonging to Class II. It is an organophosphate insecticide formerly used for fleas control but remains toxic for aquatic organisms [77]. (Mohammadreza Mohammadi Nilash et al.) Installed and electrospinning a new terpolymer nanofiber in order to quantify the amount of diazinon in fruit juice and water samples. The synthesized terpolymer and the prepared nanofiber were characterized using 1H NMR spectroscopy, scanning electron microscopy, FTIR spectroscopy, and gel permeation chromatography. The potential performance of terpolymer nanofiber, prepared as a sorbent for micro solid-phase extraction was investigated for the extraction of diazinon from aqueous media. Then, the target analytes were desorbed from the coating with an organic solvent and analyzed by gas chromatography with a flame ionization detector. The µ-SPE demonstrated good extraction efficiency for the DZ due to its large surface area and the good resistance of the prepared terpolymer nanofiber. It should be noted that this method is simple, cheap, interesting, and efficient. Furthermore, it appears that this method has excellent potential for the future of extraction techniques [47]. as well, (Yunhee Lee et al.) conducted a study for degradation organophosphates diazinon in water, utilizing microplasma equipment to produce ozone, and the authentication of their products was studied by using liquid chromatography-mass spectrometry (LC-MS). The products formed during the process were identified and determined using precise mass measurements and spectra MS/MS, providing authoritative structural determination. The pesticide reduction method utilizing ozone plasma introduced in this study may be widely used for evaluating the decomposition efficiency of pesticide residues in water and foods [48]. In 2020, (R. Mohammadzaheri et al.) conducted a study to validate a simple dispersive liquid-liquid microextraction (DLLME) for the preparation of urine samples to be analyzed for diazinon with high-performance liquid chromatography with a diode-array detector (HPLC-DAD) to ascertain diazinon exposure and intoxication. To do that, they first determined critical parameters (type and volume of extraction and disperser solvents, surfactant, pH, and salt concentrations) in preliminary experiments and then utilized central composite design to identify the best experimental conditions for DLLME-HPLC-DAD. The suggested method was precise, accurate sensitive, and linear over a broad range of diazinon concentrations in urine samples. This method can be used for diazinon analysis in routine clinical and forensic toxicology settings [49].

5.3. Detection of Carbamate pesticides: Carbamate pesticides are very important in the domain of insect control. The introduction of carbamates has led to the need for a sensitive method for the analysis of carbamates in agricultural products. The method for the determination of carbamates by colorimetry, oscillographic polarography, the combination of thin-layer chromatography and ultraviolet spectrometry, and cholinesterase inhibition technique [78].

liquid chromatography, electrochemical detection, liquid chromatography with post-column fluorescence derivatization, high-performance thin-layer chromatography, and liquid chromatography with different mass spectrometry. Of all the instrumental methods, the LC-MS system that combines the separation capability of liquid chromatography along with the sensitivity and specificity of detection from mass spectrometry and abandoned the additional derivation procedure of the entire analysis process has been generalized for pesticide residue analysis. Within the different mass spectrometers, the ion trap triple quadrupole mass spectrometer lets up multiple reaction monitoring (MRM) scan modes as an ascending tool to estimate trace quantities of pesticide residues [79].

5.3.1. Carbaryl: Carbaryl is a wide spectrum N-methylcarbamate insecticide applied globally for the control of agricultural and structural pests and as a molluscicide. Carbaryl has a low resistance in the outside environment. Human exposure to carbaryl happens through residues in food, skin contact, and air dispersion [80]. In 2019, (Zhiliang Zhang et al.) employed a versatile approach to making a flexible

SERS substrate for highly sensitive detection of carbaryl pesticides, utilizing in-situ cultivated silver nanoparticles (AgNPs) on non-woven (NW) fabric surfaces based on mussel-inspired polydopamine (PDA) molecules. The obtained NW@PDA@AgNPs fabrics demonstrated extremely sensitive and reproducible SERS signals. More importantly, these NW@PDA@AgNPs fabrics could be directly utilized as flexible SERS substrates for the rapid extraction and detection of traces of carbaryl pesticides from the surface of apples, oranges, and bananas using a simple swab approach. Analysis results fully proved that the NW@PDA@AgNPs fabrics could serve as flexible SERS substrates to efficiently collect the carbaryl pesticides and provide satisfactory quantitative analysis results [50]. Sutarnthip Ruengprapavut et al. compared the efficiency of five washing solutions (NaHCO3, NaCl, KMnO4, Deionized water, and acetic acid) on the elimination of carbaryl residues in chili and cucumber utilizing the HPLC technique. The results demonstrated that KMnO4 was the most efficient in eliminating carbaryl from the two vegetables. DI water washing was the less efficient method to remove carbaryl residues. These results will motivate producers to utilize washing with chemical solutions to reduce carbaryl contamination [51]. Nora Abdullah AlFaris Developed an ultra-performance liquid chromatography-tandem mass spectrometry method (UPLC–MS/MS) and a sensitive liquid-liquid extraction for the detection of carbaryl residues in fresh vegetables. Samples were taken from cucumber, lettuce, and spinach prepared and analyzed for 15 days to know the amount of carbaryl residue. All analytical conditioning parameters show the accuracy of the suggested UPLC-MS/MS method. The validation study confirms that the method is effective for the successful analysis of carbaryl in fresh vegetables [52].

5.3.2. Carbofuran: Carbofuran is a crystalline solid white odorless. Skin contact may cause skin and eye burns. It can emit toxic oxides of nitrogen when exposed to flames or heat. It is toxic by ingestion, skin contact, and inhalation. It is applied as a pesticide [81]. Utilizing for leaf treatment of vegetable, fruit, and field crops, commercial ornamentals, cotton, and around poultry houses and dairies. Yong He et al. conducted a study regarding the analysis of the residues of carbofuran (CBF) in the soil. These residues a difficult issue that causes soil hardness and pollution. This paper describes a very simple method via enhanced reduction of chloroauric acid by the trisodium citrate method for the manufacture of gold nanoparticles (AuNP). In a practical application, residues of CBF in soil were successfully detected by SERS with the flexible colloids of AuNPs [53]. As well, (Vijay Kumar et al.) studied the interaction of carbofuran with food grains (maize, black pulse, pea, gram, wheat, and soybean) by the UV- spectrophotometric technique. In this study, they have studied the recovery, formulation, and residual analysis by using the UV-spectrophotometric technique. The linear relationship between concentration and UV absorbance of carbofuran showed a useful analytical method for the determination of carbofuran in food grains [54]. In 2020, (Celina M. Miyazaki et al.) Combined electrochemically reduced graphene oxide and Layer-by-Layer films of magnetite nanoparticles for carbofuran detection. Show up CBF residues in oranges, sweet potatoes, lettuce, peppers, grapes, and others. This study was developed an electrochemical non-enzymatic sensor for rapid and low-cost detection of CBF [55].

5.4. Detection of pyrethroids pesticides: Several analytical tools have been employed so far for detecting pyrethroids substances. The most common methods involve GC, HPLC, SFC, GC-MS, GC-MS/MS, LC-MS, and LC-MS/MS [82], the QuEChERS (quick, easy, cheap, effective, rugged, and safe method) [83], and surface-enhanced Raman scattering (SERS)-based immunochromatographic assay (ICA) method [84].

5.4.1. Cypermethrin Cypermethrin is a synthetic pyrethroid insecticide utilizing to control many pests, especially moths in cotton, vegetable crops and fruit. It is also used in the treatment of cracks, crevices and stains to control insect pests in stores, industrial buildings, laboratories, as well as on boats, buses and airplanes. It can also be used in nursing homes, hospitals, restaurants, food processing plants, and as an insect barrier treatment for horses [85].

Charity Kanyika-Mbewe et al. determined the levels of this insecticide in Lisungwi, Neno District, a cotton-growing area in Southern Malawi. Soil samples and water samples were collected. UV/Vis spectrophotometer was used to detect cypermethrin. Cypermethrin concentration in water samples was above the recommended limits by the WHO and in the soil samples was below the recommended limits [56]. Also, (Ihsan M Shaheed et al.) conduct a study on synthetic pyrethroid, Alpha-cypermethrin (α-CY), which was determined in both river water samples collected from different agricultural areas in Kerbala city / Iraq. The method is based on the development of the analysis using high-performance liquid chromatography (HPLC) with ultraviolet detection. Dispersive liquid-liquid microextraction (DLLME) was also developed to extract α-cypermethrin from river water samples. This method may be used successfully for the analysis of α-cypermethrin in water samples [57].

5.4.2. Fenvalerate: Fenvalerate is one of the more commonly utilized pyrethroids. It is chiefly applied to control various insects and mites that infest cotton, greenstuff, fruit plants, and other crops. Fenvalerate is an environmental endocrine disruptor and a neurodevelopmental toxicant. A first report revealed that exposure to high doses of fenvalerate at puberty altered cognitive and behavioral development [86]. In 2020, (Yang Yang et al.) aimed to further investigate the effect of exposure to low-dose fenvalerate on cognitive and behavioral development. Mice were given fenvalerate orally daily starting on a postnatal day. Learning and memory were assessed by Morris water maze. Anxiety-related activities were detected by open-field and elevated plus-maze. Increased anxiety activities were observed only in females exposed to fenvalerate. There is evidence that exposure to low-dose fenvalerate impairs behavioral and cognitive development in a gender-dependent manner [87]. As well in the same year, (Fatemeh Yousefnezhad Malekia et al.) determined the quantities of Fenvalerate residue in grapes by the vortex-assisted surfactant-enhanced emulsification liquid-liquid microextraction (VSLLME) method. the combination of this method and HPLC led to a very good limit of detection (LOD at ng ml). This method VSLLME-HPLC can be utilizing to identify and determine the very low concentrations of Fenvalerate in grapes [58].

5.4.3. Pyrethrins: Pyrethrins are natural compounds with insecticidal proprieties found in the pyrethrum extract of some chrysanthemum flowers. Pyrethrins are frequently utilizing in insect control products for domestic animals or livestock and in household insecticides [59]. Also, Xinxian Qin et al. conducted a simple and accurate analytical approach for the identification of residues cinerin I, cinerin II, pyrethrin I and pyrethrin II, jasmolin I, jasmolin II,(six active ingredients of pyrethrins) in fresh and dried goji berries. was analyzed by gas chromatography with tandem mass spectrometry. Method validation is a necessary condition for obtaining reliable detection results. The method developed for the determination of pyrethrins in goji berries was validated for performance according to a conventional validation procedure which included the following parameters: linearity, LOD, LOQ, matrix effect (ME), accuracy, and precision [60].

5.4.4. Fluvalinate: Fluvalinate is a pyrethroid synthetic currently used to control varroa mites in honey bee colonies. Fluvalinate is a stable and non-volatile, fat-soluble compound [88]. Aleš Gregorc et al. conducted a study of the fluvalinate level in wax and honey after treatment of bee colonies with the following veterinary preparations has been studied: Tanis, Acaricidal bath, Varroplast M. Bee colonies were treated with drugs according to the application instructions. 7 days after treatment, wax and honey samples were taken from each colony and studied for active substance using gas-liquid chromatography. A study does not reveal any fluvalinate residues in samples of honey and wax after the treatment of bee colonies with Tanis. and a significant number of fluvalinate was found in samples honey and wax after treated with Varroplast M and also In Acaricidal bath [61].

6. Conclusion

The SERS is a powerful technique for the direct and rapid detection of pesticides due to its non-destructive nature, high sensitivity, absence of interference with water, narrow spectroscopic footprint, and easy sample preparation. Our study shows that by using SERS, all types of pesticides (endosulfan, diazinon and carbaryl, DDT ...) can be quantitatively measured and qualitatively distinguished and characterized. In a few simple sample preparation steps, a minute amount of pesticides in the samples can be rapidly extracted and detected by SERS. Future research is needed to test other types of pesticides on vegetables and fruits, study the interferences from other compounds, and compare the SERS method with other alternative techniques such as HPLC and GC-MS. However, there are challenges in performing an in-situ analysis of contaminants in the actual food matrix. With the combination of microfluidic devices and SERS detection, the application of the SERS-microfluidic system in food contaminant analysis will accelerate in the future.

7. Future prospective

The experiment will be conducted at the Surface Spectroscopies and Surface Plasmons Photonics Group Laboratory (Instituto de Estructura de la Materia, IEM-CSIC , Madrid), to test other types of pesticides that have not yet been studied and also to compare the SERS method with theoretical techniques (DFT) for results validation.

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