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Use of Micro-Raman Instrument for the Quick Detection of Corona Virus: Effect on Society

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Abstract

Quick detection and easy determination of Corona Virus present in the sample of various cells are very essential in the present scenario. People have bassically tried to prevent the rapid spread of the epidemic disease like COVID-19 and reduce the death rate which control the economic conditions of the developing country like India as well as the developed country like United States. We use various instruments and different techniques for the detection of Corona Virus present in the sample. Micro-Raman is one of the best high end instrument used for the detection of bacteria, virus, arsenic like materials etc. in nano scale present in the sample since from last three decades. In the present situation, the widely spread COVID-19 disease caused by Corona Virus creates a pandemic situation throughout the world. According to recent scientific reports recognized by various doctors, microbiologists and virologists, the Corona Virus has been changed its character day by day and muted itself within a very short period of time. So the rapid detection of Corona Virus is very essential and treat the people as early as possible to prevent community spread. If we unable to do so, it will change its characters and will represent itself as unknown to us. These mutations provide difficulties to recognize it and unable to detect easily and not to take any action against its rapid killings to the people. Not only doctors but also statisticians, mathematicians, physicists and chemists impose their responsibilities towards the perfect detection techniques, instruments and mechanism throughout the world. Micro-Raman instrument, Surface Enhanced Raman Scattering (SERS) technology and preparation of nanoparticle based SERS active substrates are the support to prevent the easy spread and control the huge death of the people due to Corona Virus.

Key Words: Corona Virus, COVID-19, Micro-Raman, SERS, Substrate.

Introduction

The easy and quick detection techniques are the main criteria to protect the epidemic disease like COVID-19 [1] throughout the world. Death of the people due to epidemic diseases may control with the help of the discovery of various techniques as well as the high-tech instruments involved in Corona Virus. There are several reasons for the death of the people due to epidemic diseases like COVID-19 [2]. Doctors are trying to find the disease by viewing their symptoms or by doing some tests involved in the disease. In some cases the symptoms are fluctuating or stay in a very short time to the patient. So keep in mind in the various complications of the epidemic diseases doctors are always try to confirm about the disease first using advanced instruments and then he able to treat the patients accordingly. So the modern instrumentation is the key to detect the disease very quickly. As a research worker in the field of molecular spectroscopy specifically in the area of Raman Scattering, it should be mentioned the efficiency of the micro-Raman instrument as quick and easy detector [3]. Though it is a very costly instrument is widely used in the recent area of research for the overall diagnostic applications and to detect various micro/nano particles present in the sample.

Since ninety years of its discovery the “Raman Effect” still finds wide applications, especially in the field of medical research. However, despite intensive applications the intrinsic problem of “Raman Effect” is that “Raman” is a weak scattering phenomenon and spectra are often obscured by Florescence background. The hindrance from undesired Fluorescence signal leads to low sensitivity, making it difficult to record vibrational signatures of molecules even at high concentrations. The low sensitivity problem of the "Raman Effect" was eventually removed with the accidental discovery of Surface Enhanced Raman Scattering (SERS), which depicts extraordinary enhancement of Raman vibrational signatures of probe molecules. The enormous enhancement of the Raman bands adsorbed by the molecules will easily identify the presence of Corona Virus present in the sample.

The phenomena of Surface Enhanced Raman Scattering (SERS):

Vibrational spectroscopy is an important tool for molecular identification. Comparison of Raman and its complementary infrared spectroscopy have enabled the scientists to elucidate structural details, protonation effects and tautomeric preferences of complex organic and inorganic molecules over the past decades [4]. However, applications of conventional Raman spectroscopy are limited by the extremely small cross section of the Raman scattering process, which are ~ 12-14 orders of magnitude below fluorescence cross section. Therefore, in 1974, a discovery by Fleischmann and co-workers [5] from the University of Southampton, which showed unexpectedly high Raman signals from pyridine molecules on rough silver electrode, attracted considerable attention [6-8]. In that paper [5] Fleischmann et al reported an extraordinary million-fold enhancement of Raman signal from pyridine molecules when they are allowed to adsorb (from solution) onto electrochemically roughened silver electrode. In early 1976, Richard Van Duyne and David Jeanmaire from Northwestern University observed the effect [7, 8] and in 1977, M. G. Albrecht and J. A. Creighton reported similar observation [9]. This surprising discovery touched off a flurry of theoretical and experimental activities. Experiments in different laboratories gave evidence that the enormously strong Raman signals were caused by true enhancement of the Raman scattering efficiency itself and not by more scattering molecules [5-7]. Within the next few years, strongly enhanced Raman signals were reported for various probe molecules [6] when attached to "rough" coinage metal surfaces (mostly on roughened Ag, Cu, Au electrodes and colloids). The effect was named "**S**urface **E**nhanced **R**aman **S**cattering (SERS)" by Professor Richard P Van Duyne. Later, the advent of scanning probe microscopic (SPM) technique revealed that the order of "surface roughness" is in the nano dimension, which now intimately relates SERS with Nano Sciences [10]. The discovery paved the way to overcome the traditionally low sensitivity problem in Raman Spectroscopy. SERS spectroscopy has now emerged as a powerful technique not only for studying the molecules or ions at trace concentrations down to single molecule detection level [11], but also helps to understand the surface chemistry at the nano scale [12]. The discovery of SERS has produced significant impact in fields such as surface chemistry, solid state physics, inorganic chemistry of metals, electrochemistry, classical electrostatics and electromagnetic theory as applied to small metal particles, problems of radiating multipoles near metal surfaces, optics of small particles, generation of surface plasmons, surface-photon interaction and second harmonic generation from molecules and surfaces.

Micro-Raman Instrument as a Corona Virus Detecting Tool

Micro-Raman is an instrument widely used to detect the presence of bacteria, virus, proteins etc. like micro or nano organisms present in the system of bulk materials. It is the challenging job to construct a SERS active substrate adsorbed by the Corona Virus. All substrates are not SERS active and as well as not adsorbed by the Corona Virus. So, if one can select or create a SERS active substrate adsorbed by the Corona Virus then he or she can easily detect the presence of this Virus very effectively within a very short period. The Schematic diagram of the micro-Raman instrument is depicted below (Figure-1)

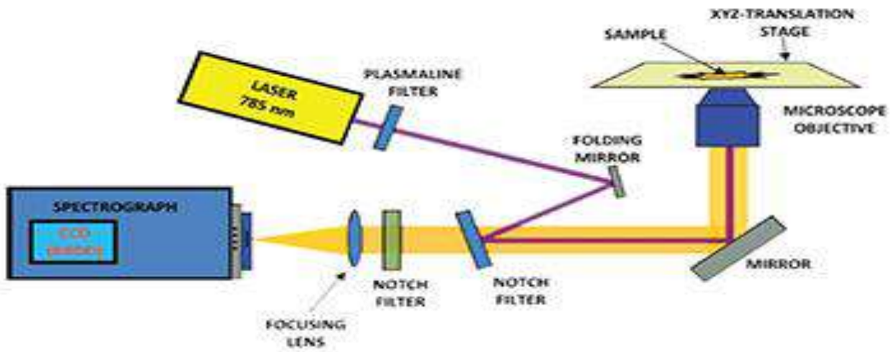

Figure-1: Schematic representation of Raman Spectrometer

When the substrate is adsorbed by the Corona Virus a sharp region will form. And on the sharp edge hot spot (Figure-2) will create and along the hot spot region a huge electromagnetic field will generate and there will be possibility of the gigantic enhancement of the Raman signal.

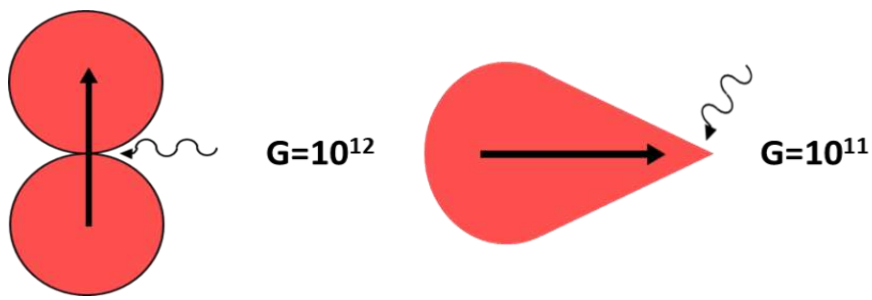

Figure-2: Formation of hot spot of various shaped sharp edge (G is the enhancement factor)

The enhancement factors (EF) 'G' of some selected Raman bands using by the Equation 1, reported elsewhere [13].

$$G = \frac{\sigma_{SERS}\,[C_{NRS}]}{\sigma_{NRS}\,[C_{SERS}]} \qquad (1)$$

Where C and σ represent the concentration and the peak area of the Raman bands measured from baseline. Here SERS represents the Surface Enhance Raman Spectra whereas NRS represents the Normal Raman Spectra.

The above theory of mechanism of enhancement of Raman bands is called electromagnetic mechanism. Another well accepted mechanism of enhancement of Raman bands is Chemical or Charge Transfer mechanism. It involves the photoinduced transfer of an electron from the Fermi level of the metal to an unoccupied molecular orbital of the adsorbate or vice versa depending on the energy of the photon and the electric potential of the interface.

SERS Techniques Applied in Diagnosis

Development in nanotechnology led to new fabrication methods for nanostructures and nanoparticles over the last decade [14]. Besides improved understanding of mechanisms that cause the signal enhancement, computational methods have been developed to modify analyte-specific nanostructures efficiently. The capacity to control the size, shape, and material of surfaces has enabled the wide application of SERS in biomedical analytics and clinical diagnostics [15]. In the review, Johannes Srajer et al [16] give a brief illustration of SERS applications with distinctive focus on cancer diagnostics, glucose detection and in vivo imaging applications. Simulation procedures were enlightened to show that electro-dynamic theory can be used to predict the features of nanostructure arrangements. A brief discussion of various fabrication methods like nanoparticle synthesis, their immobilization and lithographic techniques has been executed in the article.

For medical diagnostics, Tuan Vo-Dinh et al [17] use Raman-active dye-labeled DNA gene probes and nanostructured metallic substrates as SERS-active platforms. The surface-enhanced Raman gene probes can be used to detect DNA biotargets (e.g. gene sequences, bacterial and viral DNA) via hybridization to DNA sequences complementary to these probes. They also describe a hyper-spectral surface-enhanced Raman imaging (HSERI) system that combines imaging capabilities with SERS detection to identify cellular components with high spatial and temporal resolution. The HSERI system's application to biological imaging is demonstrated using Raman dye-labeled silver nanoparticles in cellular systems.

Resently, Pedro H.B. Aoki et al [18] presented an overview of the applications of SERS to cancer diagnosis and the detection of pesticides, explosives, and drugs (illicit and pharmacological). Several studies have been conducted to detect cancer by SERS, employing different systems and conditions to obtain adequate diagnosis. For instance, Raman detection was used to detect esophagus cancer [19], gastric cancer [20, 21], carcinoma cells [22], myeloid leukemia cells, and breastcarcinoma-derived cells [23].

Using nuclear-targeted gold nanoparticles (AuNPs) as intracellular probes Anna Huefner et al. [24] demonstrate the ability to distinguish between progenitor and differentiated cell types in a human neuroblastoma cell line using SERS. SERS spectra from the whole cell area as well as only the nucleus were analyzed using principal component analysis that allowed definite distinction of the different cell types. SERS spectra from the nuclear region showed the developments during cellular differentiation by identifying an increase in DNA/RNA ratio and proteins transcribed.

In that paper, Yun Suk Huh et al [25] reviewed the advanced in SERS based optical detection techniques with an application focus on cancer. They reported the recent advances in instrumentation and experimental design for various applications of SERS in the field of molecular diagnosis of cancer by monitoring DNA–DNA hybridizations, protein–protein interactions, and other ligand–receptor interactions. Application of SERS as a diagnostic system for hypersialylated metastatic cancers was reported by B. Shashni et al [26]. They reported on the application of phenylboronic acid-installed PEGylated gold nanoparticles coupled with Toluidine blue O (T/BA-GNPs) as SERS probes to target surface sialic acid (N-acetylneuraminic acid, Neu5Ac). Strong SERS signals from metastatic cancer cell lines (breast cancer; MDA-MB231 and colon cancer; Colon-26) were observed, contrary to non-metastatic MCF-7 cells (breast cancer).

Sarah Mc. Aughtrie et al [27] reviewed to analyses a range of diseases which can be detected by Raman or SERS, particularly those in vitro, ex vivo and in vivo. A direct consequence of the specified spectra allowed for definite identification of disease biomarkers. They clearly demonstrated the sophistication of the investigated systems varied widely but the suitability of Raman and SERS for medical diagnostics and future implementation in a clinical environment.

In that paper, Wei Xie et al [28] highlighted the selected medical applications of SERS from the past few years. Both aspects the label-free SERS detection of biomedical samples as well as the use of SERS labels in medical applications were explained. SERS applications in intracellular monitoring of thiopurine anticancer drug release, glucose sensing, identification of breast cancer stem cells, brain tumor imaging, photo-thermal therapy response of cancer cells was explained by them. They also reported that, SERS is widely used for the detection of DNA, multiplex pathogen DNA, separation-free DNA, pancreatic cancer, cholera, biological cells, bronchioalveolar stem cells, circulating tumor cells in blood, in vivo inflammation etc. Over the last five years, Hoan T. Ngo et al [29] has developed in their laboratory several chip-based DNA detection techniques including the molecular sentinel-on-chip (MSC), the multiplex MSC, and the inverse molecular sentinel-on-chip (iMS-on-Chip). Xiao-Shan Zheng et al [30] reported the differentiation of the cancerous nasopharyngeal cells from the normal nasopharyngeal cells with high diagnostic accuracy (98.7%) has been realized by using ultrasound-mediated SERS combined with (Principal Component Analysis–Linear Discriminant Analysis) PCA–LDA multivariate analysis. This experimental study establishes the great potential of ultrasound-mediated cell SERS methods for high-throughput cancer cell screening applications. Agnieszka Kamińska et al [31] reported the recent advances in SERS include innovative applications of bimolecular sensors for clinical diagnosis of various diseases by introducing Au/Si substrates exhibit good performance toward sensitive and reproducible SERS-based detection of complex human body fluids such as blood plasma, cerebrospinal fluid and urine. In that paper, Nicoleta Elena Dina et al [32] reported three different clinical isolates of relevant filamentous fungal species were discriminated by using a rapid (less than 5 min) and sensitive SERS-based detection method, assisted by chemometrics. The holistic evaluation of the SERS spectra was performed by employing appropriate chemometric tools - classical and fuzzy principal component analysis (FPCA) in combination with linear discriminant analysis (LDA) applied to the first relevant principal components. Recently Di Zhang et al [33] proposed a lateral flow assay (LFA) based on core-shell SERS nanotags for multiplex and quantitative detection of cardiac biomarkers for the early diagnosis of acute myocardial infarction (AMI).

Conclusions

To identify the death recording techniques and actual measure of the death of the people affected by the epidemic disease like COVID-19 due to infection of corona virus is a challenging effort throughout the world not only for the doctors, physicians and micro-biologists but also for the mathematicians, physicists, statisticians and chemists. Here, I have reported the process of easy and quick detection of the corona virus by which the people would not be killed by COVID-19 or any other comorbid diseases and the society may able to free from pandemic situation. The discovery of the phenomena of SERS is reported here to realize the mechanism involved for the enhancement of Raman bands which will able to easy detection of Corona Virus present in the sample. The micro-Raman instrument is widely used not only for the presence of micro species present in the sample but it is used also in various diagnostic applications through SERS activity is reported here. So, we can use the micro-Raman instrument for quick detection and identify the exact cause of death to reduce the easy spread of COVID-19 like epidemic diseases by the application of SERS technology along with the preparation of nanoparticle based SERS active substrates. In this way, the quick detection of the Corona Virus by the enhancement of Raman bands and the efficient use of the instruments involved in it, will be very much effective to control the economic conditions and the social stability not only our country like India but also throughout the world.

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