

## A REVIEW ON MATRIX-ASSISTED LASER DESORPTION/ IONIZATION TIME-OF-FLIGHT (MALDI-TOF) MASS SPECTROMETRY.

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### Abstract:

**Background:** maldi-tof mass spectrometry (ms) is an important technique that produces both qualitative and quantitative measurements of low molecular weight compounds for its rapid, reliable results. It is a recent method for bacteria identification. It is set to make in rounds into clinical chemistry because it gives advantages over other analytic platforms. These benefits include low purchase and operating costs, ease of use, ruggedness, and high throughput. When coupled with innovative front-end strategies and applied to important clinical problems, it can produce rapid, sensitive, and cost-effective assays.

**Content:** the use of maldi-tof mass spectroscopy will certainly help in the rapid identification of anything unusual. Maldi-tof mass spectroscopy has become a reference method for the routine identification of bacteria isolated in clinical microbiology laboratories around the world. Its specificity, user-friendliness, together with its ability to provide reliable results in less than 5 min has favored its implementation and further development. The measure of microbial species identified by maldi-tof routinely has risen in the last few years.

**Summary:** maldi-tofms, already changed the practice of clinical microbiology and, the analysis illustrates how and why it is now set to play a more important role in vitro diagnostics in particular, and clinical chemistry.

**Key words:** maldi-tof, ms, bacterial identification, clinical chemistry

### Definition:-

-it is a powerful analytical - mass spectrometry technique that has generated numerous diagnostic and clinical applications, especially for the identification of micro organisms for medical diagnosis.

### Introduction:-

-maldi-tof measures the mass of molecules from a sample that has been embedded in a matrix by using a laser to ablate and desorb the molecule with minimal fragmentation.

- the sample's molecules are ionized in the resultant hot plume of ablated gases and are funnelled into a tof mass spectrometer that records the ion's mass-to charge (m/z) ratio .this is achieved by measuring the time, the ions take to traverse a known length under acceleration by an electric field of known strength.

-the resultant mass spectrum is produced from the pattern (ie, position and relative intensity) of detected m/z peaks, generating a distinct profile for a particular sample. - the uniqueness of mass spectra can be leveraged for identification purpose when a comparison reference spectrum is available.

-micro-organisms are best identified using 16srna and 18srna gene sequence however, in recent years matrix assisted laser desorption ionization time of flight mass spectrometry (maldi - tofms) is widely used for microbial identification.

-by the maldi-tofms process, microbes are identified using either intact cells or extract cells .this method is very economical- and this process is rapid. This technology has been appreciated by the users who have reported usage of maldi -tof-ms for a number of purposes like identification of the microorganisms strain typing, epidemiological studies, detection of biological warfare agents. The detection of water and food borne pathogens. Detection of antibiotic resistance and detection of blood and urinary tract pathogens.

-the single colony method can be used for obtaining a protein fingerprint or profile unique to each microorganism.

- the technique has been mainly used in the clinical field, but it also has significant potential in the environmental field.

- due to its rapid and precise identification of genus and species of gram positive and gram negative bacteria matrix assisted laser desorption/ionization time of flight mass spectrometer is the most used ms instrument in biology.

In the field of mass spectroscopy:-

- maldi is one of the ionization technique that works by using the laser energy which absorbs matrix & create ions from the large molecules.

Method :-

-this method includes 3 steps:

Step 1:- sample is combined with suitable matrix plate and the formed product is applied to a metal plate.

Step 2:- a pulsed laser is used which irradiated the sample, that shows ablation and desorption action of the sample as well as matrix material.

Step 3:- finally the molecules are ionised by protonation and deprotonation in the hot plume of ablated gases.

-later they can be accelerated into whichever mass spectroscopy which is used to analyse them.

-the matrix is composed of crystallised molecules from which the most commonly used are sinapinic acid,  $\alpha$ -cyano-4-cyano-4-hydroxy. Cinnamonic acid and 2,5-dihydroxybenzoic acid.

-it has been applied to the analysis of biomolecules and various organic molecules, which tend to be fragile and fragment when ionized by more conventional ionization methods.

- it is similar to electrospray ionization (esi) in character, in that both techniques are relatively soft (low fragmentation) ways of obtaining ions of large molecules in the gas phase, through maldi typically produces far fewer multi-charged ions.

Maldi-tofms based microorganisms identification and sample preparation:-

1. A rapid, accurate and sensitive spectra of the bio analytes within a sample is provided by the maldi-tofms.
2. M/z ratio is detected by using ms.
3. M/z ratio can be determined by the tof of ions which the detector measure tof of ions to calculating masses of ions.
4. Whole cell ms (wcms) which is another name/ is called as intact cell ms is a method which acquires microorganism. Protein profile data by maldi-tofms.
5. On a maldi target plate there is a formation of single colony of bacteria or yeast from microorganisms that are smeared as thin film directly. A key to prepare sample for maldi-tofms is the removal of blood cells and proteins that are derived from the host and culture media.
6. The colony forming unit (cfu) for bacterial identification of maldi-tofms is  $\sim 10^{-10}$  cfu of e.coli.
7. The identical result can be obtained by maldi-tofms technology in hours after the colony applied for the sample preparation.

Maldi-tof based total serum protein fingerprinting for liver cancer diagnosis :-

-serum is one of the most commonly used sample in many studies to identify protein biomarkers to diagnose cancer. Although conventional enzyme-linked immunosorbent assay (elisa) or liquid chromatography-mass spectrometry (lc-ms)-based methods have been applied as clinical tools for diagnosing cancer, there have been some problems, such as inferior multiplexing capabilities, high development costs & long turnaround times, which are inappropriate for high-throughput analytical platforms.

-here, we developed a simple & robust cancer maldi-tofms based total diagnostic method using serum protein fingerprinting.

Method:-

-serum samples were simply diluted with distilled water & subsequently spotted onto a maldi plate. Without prior chromatographic separation/ purification.

- the sample preparation method was enough to collect reproducible total serum protein fingerprints & would be highly advantageous for high-throughput assay.

-each of the integrated main spectrum profiles (maps), which are representative of liver cancer patients (n=40) or healthy controls (n=80), was automatically generated by the maldi biotype 3 software.

Anti-antibiotic sensitivity test:-

It is another key of information which affect the clinical treatment. It desires to develop a fast and reliable method easing maldi-tof-ms for detecting drug sensitivity.

-ast detection principles are tested and developed such as :

- 1) ms detection of antibiotic degradation.
- 2) detection of drug resistant strain biomarkers.
- 3) detection of stable isotope- labelled -amino acids (4,5,6)

- ms is usually used to detect maldi-tofms and m/2 ratio provides an accurate, sensitive spectra of the bioanalyses within an sample, (3, 7, 8).

Advantage:-

- It is widely used in the analysis of biomolecules (carbohydrates proteins peptides dna .
- Maldiis also used in the analysis of organic molecules (polymers macromolecules).
- Major advantage of using maldi-tofms is time normally logical are going to common normally logical are going to common ms it's time saving bacterial identification is performed in less than hour as opposed to 24 to 48 hrs.

Disadvantage :-

- The throwback of this technology is that identification of new isolates is possible only if the spectral database contains peptide mass fingerprints of the type strains of specific genera/species/subspecies strains.

Applications:-

Detection of protein complexes :-

Initial observations that some peptide-peptide complexes could survive maldi deposition & ionization.

Parasitology:-

-maldi-tof spectra have been used for the detection of various parasites such as plasmodium, trypanosomes .in addition to these unicellular parasites, maldi/tof can be used for the identification of parasitic insects such as lice, the free swimming stage of trematodes.

Microbiology :-

-used for the identification of microorganisms such as ,bacteria & fungi.

-a high resolution of maldi-ms performed on a fourier transform ion cyclotron resonance ms (ft-ms) have been demonstrated for typing & subtyping visas though single ion detection known as prototyping, with a particular focus on influenza virus.

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