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# Field Emission Scanning Electron Microscopy (Fesem) with A Very Big Future in Pharmaceutical Research

**R. Senthil Prabhu*, R. Priyanka, M. Vijay and G.R. Kaviya Vikashini**

**Department of Pharmaceutics, College of Pharmacy, Madurai Medical College, Madurai.**
**Affiliated to The Tamil Nadu Dr. M.G. R Medical University, Chennai-32. Tamil Nadu.**

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***Corresponding Author Email:** grsprabhu24@yahoo.com

## Abstract
Field Emission Scanning Electron Microscope (FESEM) is a microscope that works with electrons (particles with negative charge) instead of light. These electrons are liberated by a field emission source. The object is scanned by electrons according to a zig-zag pattern. The Field Emission Scanning Electron Microscope (FESEM) provides ultra-high imaging at low accelerating voltages and small working distances. It provides resolution of the images is a low as 0.6nm at 15KV and 1.2nm at 1 kV, allowing examination of the top surface of nano powders, nanofilm and nanofiber in the wide range of applications such as mineralogy, ceramics, polymer, metallurgy, electronic device, chemistry, physics and life sciences. This system is equipped with several detectors to detect various signals such as secondary electrons (SE) detector for topographic information and back-scattered electrons (BSE) detector for materials composition contrast. Field emission SEM (FESEM) produces clear, less electro statically distorted images with spatial resolution down to 11/2 nanometer- three to six times better. Although FESEM, are large, expensive pieces of equipment. They remain popular among researchers due to their wide range of application and capabilities including the high resolution, three dimensional, detailed images they produce. This review describes about the instrumentation, operation and pharmaceutical applications with respective drug release.

**Keywords**
FESEM, instrumentation, drug release, applications.

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## INTRODUCTION
There are many mechanisms by which the drug release can be controlled in a system: dissolution, diffusion, osmosis, partitioning, swelling, erosion, and targeting. They are dependent on the application and may act simultaneously or at different stages of a process of delivery [1]. It is common for a system or device to present more than one of them, but the classification of the mechanism of release is based on the main mechanism. The drug release from pharmaceutical oral solid dosage forms having major impact in bioavailability of drugs. There are two types of drug release mechanism mainly Drug dissolution and diffusion [2].

- Drug dissolution: Dissolution refers to the process by which s solid phase (e.g., a tablet or powder) goes into a solution phase such as water. It is the process for which drug molecules leave the boundary surrounding the dosage form and diffuses into the dissolution media.
- Drug diffusion: Drug diffuses across the cell membrane from a region of high concentration to

the region of low concentration. Diffusion rate is directly proportional to the gradient but also depends upon on the molecules, lipid solubility, size, degree of ionization and the area of absorptive surface [3].

*In –vitro* drug release studies alone will not be able to predict the type of drug release mechanism and the changes in very fine surface features and coating material properties on oral solid dosage forms. Further this can be absolutely predicted by using FESEM images [4]. This present work discusses extensively on background of instrumentation, operation, and various applications about FESEM.

**BACKGROUND OF FESEM**

The first true scanning electron microscope (SEM) was described and evolved in 1942 by Zworykin, who exhibited that secondary electrons (SE) provide topographic contrast by biasing the collector positively relative to the specimen and reached the resolution of 50 nm when using an electron multiplier tube as a pre- amplifier of the SE emission current. The only electron source designed for high-resolution imaging for various kinds of materials is field emission, which use field emitter gun (FEG) to emit electrons [5]. The SEM that uses FEG as the emitter type is called Field emission scanning microscope (FESEM); whereby the emitter type is used as part of its name to distinguish it from the classic SEM. FESEM is an advanced microscope offering increased magnification and the ability to observe very fine features at a lower voltage than the SEM found in most research laboratories.

A FESEM is used to visualize very small topographic details on the surface or entire or fractioned objects. Researchers in biology, chemistry, and physics apply this technique to observe structures that may be as small as 1 nanometer (= billion of a millimeter). The FESEM may be employed to study organelles and DNA material in cells, synthetic polymers, and coatings on microchips. The Field Emission Scanning Electron Microscope (FESEM) has a much brighter electron source and smaller beam size than a typical SEM increasing the useful magnification of observation and imaging up to 500000x. [6]. A second advantage of the FESEM is that high resolution imaging can be performed with very low accelerating voltages. This enhances the observation of very fine surface features, electron beam sensitive materials, and non-conductive materials.

Field emission scanning electron microscopy (FESEM) provides topographical and elemental information at magnifications of 10x to 3000,000x, with virtually unlimited depth of field. Compared with convention scanning electron microscopy (SEM) , field emission SEM (FESEM) produces clear, less electro statically distorted images with spatial resolution down to 11/2 nanometer- three to six times better [7].

**ADVANTAGES**

- The ability to scan smaller area contamination spots at electron accelerating voltages compatible with energy dispersive spectroscopy [8].
- Reduced penetration of low kinetic energy electrons probes closer to the immediate material surface.
- High quality, low voltage images with negligible electrical charging of samples accelerating voltages ranging from 0.5kv to 30kv [9].
- Essentially no need for placing conducting coatings on insulating materials.
- Observation of very fine surface features of coating materials and pharmaceutical dosage forms [10].

**PRINCIPLE OF OPERATION**

FESEM uses a focused beam of electrons to generate an image or to analyze the specimen as represent in Figure 1. For operation, the gun head, the column and specimen chamber have to be evacuated. The pre-vacuum pump and turbo pump evacuate the specimen chamber [11]. Vacuum in the specimen chamber is measure by penning gauge. Column chamber value remains closed until the detected pressure is not ready for operation. After vent command, column chamber value closes and $N_2$ gas flows into the specimen chamber through vent value [12]. A field emission cathode in the electron gun of a scanning electron microscope provides narrower probing beams at low as well as high electron energy, resulting in both improved spatial resolution and minimized sample charging and damage. For applications that demand the highest magnification possible [13].

**INSTRUMENTATION**

The Field Emission Scanning Electron Microscope (FESEM) is an instrument which, just like the SEM, provides a wide variety of information from the sample surface, but with higher resolution and a much greater energy range [14]. It works just like a conventional SEM; the sample surface is scanned with an electron beam while a monitor displays the information that interests us on the basis of the detectors available [15].

The biggest difference between a FESEM and a SEM lies in the electron generation system. As a source of electrons, the FESEM uses a field emission gun that provides extremely focused high and low energy electron beams, which greatly improves spatial resolution and enables work to be carried out at very low potential (0.02-5kv) this helps to minimize the charging effect on non-conductive specimens and to avoid damage to electron beam sensitive samples [16]. Another highly remarkable feature of FESEM is its use of in-lens detectors. These detectors, which are optimized to work at high resolution and very low acceleration potential, are fundamental for getting the maximum performances from the equipment as shown in Figure 2.

**Figure 1: Principle of Operation of FESEM**

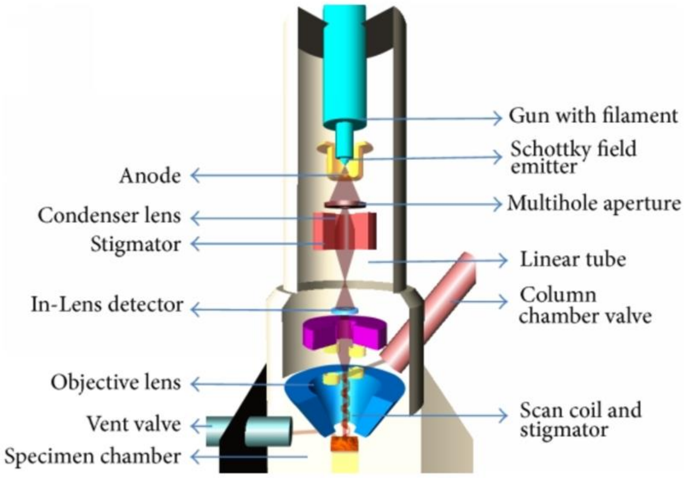
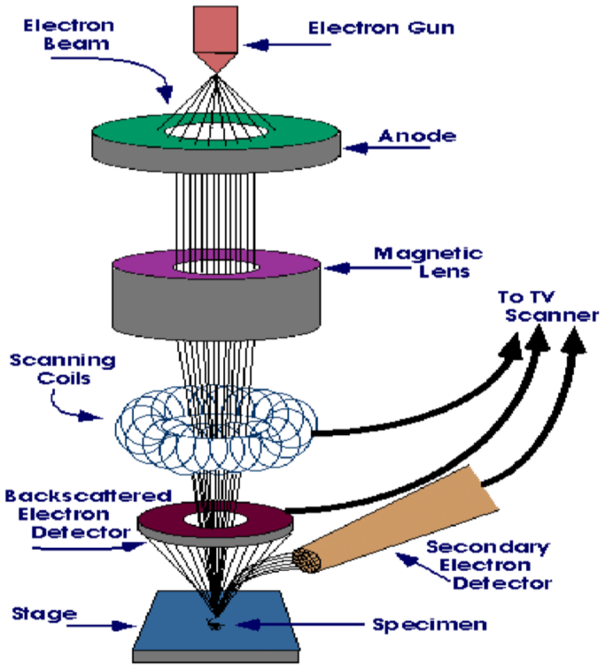



**Figure 2: Schematic Diagram of FESEM**




**SAMPLE REQUIREMENT FOR FESEM**

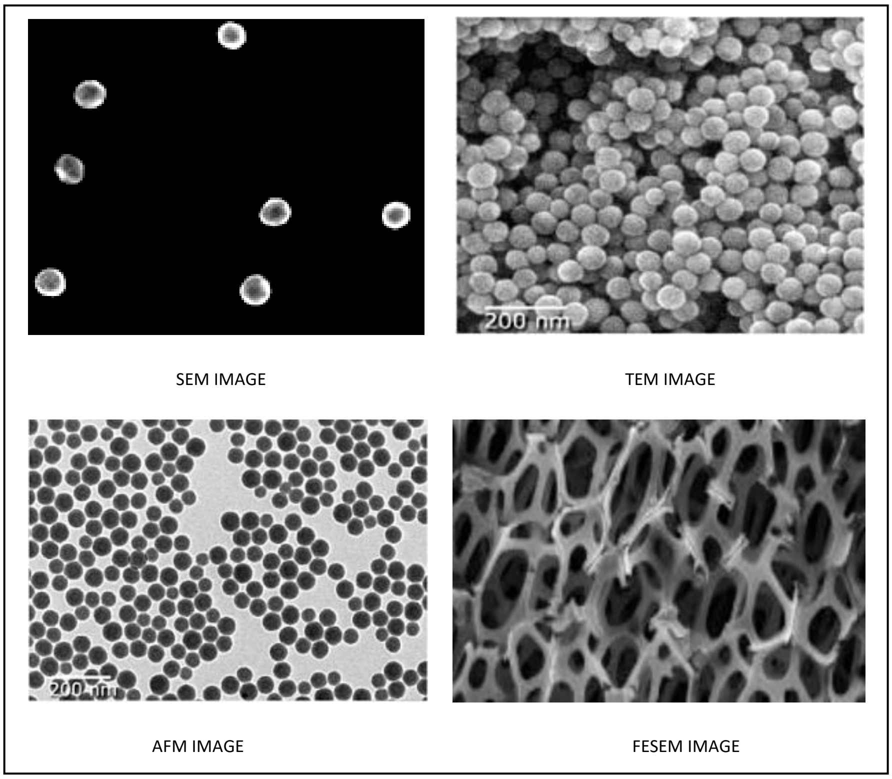
- Sample should be dry and non- magnetic [17].
- Powder/ metal/ thin films samples are accepted for analysis. If powder samples have > 100 nm particle, user is expected to dissolve the same in appropriate solvent and then drop cast/spin coat it on conducting substrate. E.g., Copper. Aluminum foil, Silicon substrate before handling for analysis. This can be discussed with the operator [18].
- Biological and liquid samples should be fixed and coated/ drop casted on conducting

substrates (1cm) and dried well before the allotted slot timings. [19-21]
- 10 mg minimum quantity of sample required.

**APPLICATIONS OF FESEM**
- Semiconductor device cross section analyses for gate widths, gate oxides, film thickness, and construction details.
- Advanced coating thickness and structure uniformity determination
- Small contamination feature geometry and elemental composition measurement.
- Microscopic feature measurements
- Corrosion evaluations
- Spray dried Powders evaluations
- Transdermal Film evaluations
- Striation measurements for high cycle fatigue fractures
- Coating evaluations in tablets
- Characterization of exceptionally fine specimen features
- Fracture characterization for polymers and very small components
- Surface contamination analysis
- Small component material analysis
- Laser and resistance weld evaluation
- Printed and integrated circuit analysis
- Microstructure studies [22].

A FESEM is used to visualize very small topographic details on the surface (or) fractionized objects [23]. Researchers in various fields applied this technique to observe structures that may be as small as (1nm = billion of a mm). FESEM has much higher resolution than SEM, TEM and AFM [24]. FESEM allows large amount of sample to be analyzed at a time and can see the 3D structure of the sample as shown in figure 3.

**Figure 3: Comparison of high-resolution images of SEM, TEM, AFM and FESEM nanoparticles.**




**CONCLUSION**

The Field Emission Scanning Electron Microscope is a type of electron microscope that images the sample surface by scanning it with high energy beam of electrons in a raster scan pattern enabling the investigation of conductive, non-conductive, and high vacuum incompatible materials. The Field Emission Scanning Electron Microscope is a versatile high resolution scanning electron microscope. It can provide stable large probe current- to deliver ultrahigh resolution with wide range of probe currents for all applications. Based on the review it was concluded that FESEM can be used as a promising tool in observation of very fine surface features of oral solid dosage forms on drug release mechanism. Understanding principle of work of both secondary electron imaging and backscattered electron imaging features is very important to have a complete knowledge on how FESEM instrument work.

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