

## MODIFICATION OF DRUG-DELIVERY PARTICLE SIZES TO THE MICRO AND NANO RANGE

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### ABSTRACT

*The need for food that does not include any additives has created a unique opportunity for antimicrobial food packaging films. Antimicrobial food packaging has a substantial impact on the safety of food because it inhibits the growth of microorganisms that break down food. Antimicrobial packaging's primary purpose is to lengthen the amount of time that food products may be stored without going bad. Nano composite films have special mechanical, thermal, and barrier properties. Nano composite films also have these qualities. The use of antimicrobial nanofiller may result in the development of antibacterial properties. Inorganic antibacterial nanofillers are better for the environment than organic ones when it comes to the production of nanocomposite films.*

**Keywords:-** Drug-Delivery, Micro And Nano Range.

### INTRODUCTION

#### BACKGROUND

The present trend in food technology is toward the production of healthier processed foods, which involves the use of the fewest possible chemical additives. A variety of antimicrobial compounds are often used with food formulations in order to extend the shelf life of foods and to inhibit the development of microorganisms. When antimicrobial (organic) agents are directly blended into food composition, the efficacy of the antimicrobial is nullified because the antimicrobial establishes complicated interactions with the food components. Consumers are exposed to a heightened danger to their health as a result of this

behavior. However, this conventional approach is not suitable for the current trend in food technology, which aims to produce processed meals that are healthier by reducing the quantities of chemical additives they contain.

### PACKAGING FOR ACTIVE FOOD

The phrase "active packaging technology" refers to situations in which food packaging systems fulfill functions in addition to those typically associated with packaging. An active packaging system is a revolutionary packaging method that is the result of a combination of materials science and engineering. This combination led to the development of the approach.

### AN OVERVIEW OF ANTIMICROBIAL FOOD PACKAGING

The development of microbes on the surface of food is what causes it to go bad, but the process may be stopped by employing antimicrobial treatments. The antimicrobial properties of food packaging prolong the lag phase of the bacteria, so preventing their growth.

Organic antimicrobial agents are used in food packaging in order to restrict the development of microorganisms and to increase the acceptability of the food. On the other hand, inorganic antimicrobial agents are appropriate for maintaining the stability and safety of the process.

On the other hand, certain organic antibacterial agents are made of a synthetic substance that might have negative repercussions for the health of consumers and can impart an unpleasant taste. Antimicrobial food packaging solutions have recently gotten off the ground as a means of contributing to the resolution of these issues.

### **The Use of Antimicrobial Agents in the Packaging of Antimicrobial Food**

Organic and inorganic materials are the two primary classifications that are used for classifying antibacterial agents. The term "organics antimicrobial agents" refers to naturally occurring substances like chitosan and chitin, as well as plant extracts, halogenated compounds, quaternary ammonium salts, and phenols, all of which have recently garnered a great deal of attention.

In terms of inorganic agents, the last group contained things like metals, metal oxides, and metals bound with phosphates. As a result of their ability to withstand severe processing conditions and to exert beneficial antimicrobial effects against food-borne pathogens, they have attracted a great deal of attention.

#### **Modification of particle sizes:**

##### **Advantages of modifying particle sizes:**

Modifying the size of the drug-delivery particles' particles might potentially confer a variety of advantages on the formulation as a whole. Consider for instance the following:

The use of smaller particles, which are capable of penetrating deeper into tissues and cells, results in an improvement in the efficiency of the pharmaceutical administration process.

The rate at which a drug is released from smaller particles may be boosted due to the

fact that smaller particles have a larger ratio of surface area to volume.

When it comes to the manufacturing process and the formulation, it could be easier to deal with particles that are of a greater size.

**Microfluidic devices:** As used in this particular setting, the word "microfluidics" refers to the manipulation of fluids on a scale that is often measured in micrometers, and it is the application of this term that is being discussed. They have been put to use in the process of diagnosing diseases, dispensing drugs, and conducting research in a variety of biological fields.

**Nanoparticles:** These particles, the majority of which have a size that is less than 100 nanometers, have a particular set of features that are unique to them because of their diminutive size. Imaging technologies, the administration of medications, and the storage of energy are among of the areas that have discovered applications for them.

**Nanotubes:** The diameter of these structures is on the order of a few nanometers, and their overall form is cylindrical. They are composed of individual atoms of the element carbon. They are used in the electrical sector, in the storage of energy, and as reinforcements in composite materials because to the high conductivity and strength that they possess.

**Nano-electronics:** Nanofabrication is the process of designing and creating electronic components with a size of one nanometer or less, and the term refers to both the method and the term itself. Nanowires, nanotransistors, and nanocircuits are all types of components

that are included into it, and each of these terms refers to a different component.

**Micro-optics:** These are optical components that have been created and manufactured, and the units of measurement used to describe their size are micrometers. Microlenses, microprisms, and micromirrors are a few examples of the kinds of microoptical components that find utility in a wide variety of different applications. Sensing, imaging biomedicine, and wireless communication are only a few examples of the many uses for these technologies.

**Overall action of inorganic antimicrobials on microorganisms that cause food poisoning**

Inorganic antimicrobial compounds, similar to antibiotics, may use the metal transference system and metalloproteins of bacteria to distinguish bacterial cells from mammalian cells. Antibacterial capabilities might be demonstrated by inorganic antimicrobial compounds via a variety of methods.

The number of customers looking for meals that are pre-packaged, hermetically sealed, and have a long shelf life has been steadily rising. The process of preparing food culminates in the packaging of the finished product. The finished product may be stored for a period of time using food preservation techniques; nevertheless, there is always the possibility that it will get contaminated. There is some evidence that antimicrobial coatings on food packaging sheets can significantly increase the shelf life of the food and reduce the risk of recontamination.

In order to impart an antibacterial quality onto films, polymer matrices may have compounds with antimicrobial properties added to them. Since they are able to

endure the rigorous manufacturing conditions of polymer films, inorganic antimicrobial chemicals such as metal and metal oxides have an advantage over organic antibacterial agents such as organic acids, bacteriocins, enzymes, and spice extracts.

The food industry makes extensive use of polymers derived from petrochemicals due to the low cost of these materials, the ease with which they can be obtained, and the functional benefits that they provide. In addition to being flexible and suitable for consumption, these materials are also transparent, affordable, adaptable, and safe. In comparison to other types of packaging materials, the use of polymeric films in the packaging of food is far more common.

**EXPERIMENTAL**

**Resources and Procedures**

**Table- Materials utilized in the manufacture of LDPE/Cu nanocomposite film and Cu-NPs**

Sr. No	Name of Chemical	Molecular weight (g/mole)	Density (g/cm <sup>3</sup> )	Purity	Manufacturer
1	Copper sulphate dehydrated (CuSO <sub>4</sub> )	159.609	3.6	98%	Loba Chemical,
2	Ascorbic acid (C <sub>6</sub> H <sub>8</sub> O <sub>6</sub> )	176.12	1.65	99%	Merck
3	Gelatin	-	-	Extra pure	Himedia
4	Xylene GR (C <sub>8</sub> H <sub>10</sub> )	106.16	0.861	99.9%	Merck

5	Cyclohexanone (C <sub>6</sub> H <sub>10</sub> O)	98.15	0.9478	99.9%	Merck
6	Low density polyethylene (LDPE)	50,000	0.917	-	Reliance industries

### Synthesis Of Cu-NPs

The use of a microwave allowed for the production of Cu-NPs that were very pure and had a size of 50 nm. The synthesis required the mixing of 10 milliliters of 0.1 M CuSO<sub>4</sub>, 50 milliliters of 1% gelatin solution, and 5 milliliters of 0.1 M ascorbic acid. When spun by a mechanical device, the color shifts from blue to green at room temperature.

After that, the liquid was brought to a boil in a microwave oven for a total of two to three cycles of around thirty seconds on and off. The green color of the solution was gradually overtaken by the hues of yellow, orange, and finally wine-red caused by the Cu-NPs. Wet Cu-NPs were synthesized during centrifugations that lasted for ten minutes and used a speed of 10,000 revolutions per minute. After that, they were heated to 50 degrees for 24 hours while being dried in a vacuum.

### LDPE/Cu Nanocomposite Film Creation

Solvent evaporation was used to produce LDPE/Cu nanocomposites with concentrations of 0.5, 1, 1.5, 2, 2.5, and 3 weight percent, and a doctor blade film applicator was used to produce thin films with uniform thickness. Using a temperature-controlled ultrasonic bath sonicator, the Cu-NPs were appropriately dispersed in the LDPE/xylene solution prior to the creation of the films. This was done before 5 grams of LDPE polymer

were dissolved in 45 milliliters of xylene at a temperature that remained constant at 110 degrees Celsius.

After that, composite films were made on glass plates by using a doctor blade film applicator and heating them to 100 degrees Celsius (120 microns). LDPE, a highly crystalline polymer, will begin to precipitate as soon as the temperature of the xylene falls below 150 (5) degrees Celsius. The temperature of the glass plate used in the production of the film was maintained at 150 degrees Celsius. When the films had been prepared, they were taken from the glass plates.

### CHARACTERIZATION

#### Functional and Optical Properties

In order to explore the optical characteristics of Cu-NPs, UV-Vis spectra were measured using an Agilent Technologies Cary 60 UV-VIS spectrophotometer. This instrument measures wavelengths in the range of 200 nm to 800 nm. Following every 30 second cycle in the microwave, the sample was looked at to ensure that the Cu-NPs were forming in the correct manner. In order to assess the functional composition of the Cu-NPs that had gelatin caps, Fourier transform infrared spectroscopy was used to investigate the samples (FTIR). Recordings of FTIR spectra were made of gelatin-capped Cu-NPs using a Japanese 8400 Shimadzu instrument. In the frequency range of 400–4000 cm<sup>-1</sup>, both the number of scans performed on each sample, which was kept at 25, and the computation resolution, which was also kept at 4 cm<sup>-1</sup>, were maintained.

#### Radiation Diffraction (XRD)

Using XRD with monochromatic Cu Ka radiation (1.5406 Å) at 40 kV and 40 mA, we were able to identify the

crystalline structure of Cu-NPs as well as the LDPE/Cu nanocomposite film (Model D8 Advance Bruker Limited Germany). The diffraction pattern optimization process was carried out at a scanning speed of 10 S-1 and an angular range of 5-80(2 theta).

#### **Aspects of morphology and particle size**

Hitachi High Technology Company Ltd. in Japan was responsible for taking the FE-SEM images of the Cu-NPs and nanocomposites films that were taken with their FE-SEM S-4800 Type II instrument. The surface morphology, elemental compositions, and particle sizes were all analyzed with the help of these photographs. The energy that was being used was 15.0 KeV.

After being covered in gold and mounted on a specimen stub, the copper nanoparticles (Cu-NPs) and the LDPE/cu nanocomposite film were prepared to be analyzed using a microscope. The elemental compositions of the samples were determined with the use of EDS. It was determined with the use of a particle size analyzer what the size of the Cu-NPs particles was (Malvern, ZS- 200, Worcestershire UK). The dissolution of the Cu-NPs in distilled water served the purpose of determining the particle size distribution.

#### **Thermal Features**

Both a Shimadzu TGA 50 thermogravimetric analyzer and a Shimadzu DSC 60 thermogravimetric analyzer, both manufactured in Japan, were utilized in order to investigate the thermal properties of LDPE/Cu nanocomposite films. Programming of temperatures was done between 35 and 180 degrees Celsius at a heating rate of 20 degrees Celsius per minute, all while

nitrogen flowed through the system at a rate of 50 milliliters per minute.

#### **Novel Polystyrene Antimicrobial Food Packaging Film Functionalized By Chitosan-Tio<sub>2</sub> Nanoparticles**

The declining incidence of foodborne illnesses provides impetus for the development of antimicrobial coatings for food packaging. a one-of-a-kind material for use in food packaging that has the potential to kill bacteria, so improving the quality of the food, extending its shelf life, and preventing or delaying the process of rotting. It is possible to achieve an antibacterial impact by increasing the amount of antimicrobials present in either the polymer matrix or the area around the meal.

It has been established that inorganic antimicrobial compounds are more effective than organic antibacterial agents due to the fact that inorganic antimicrobial compounds can endure demanding production circumstances. In contrast to the latter, which is mostly made up of organic acids, enzymes, and polymers, the former comprises of metal or metal oxide nanoparticles. The use of nanoparticles in the packaging of food has seen a significant uptick recently.

The incorporation of nanoparticles into the matrix of polymer films results in improvements to the films' physicochemical qualities. The term "active food packaging technology" is used to refer to this idea. Despite the fact that the technology for deploying metal and metal oxide nanoparticles as antibacterial in food packaging is well established, there is still a concern that consuming metal ions that may have found their way into food might cause harm.

#### **EXPERIMENTAL**

## Materials and Procedures

Table contains a list of the materials utilized in the experiment's efforts.

**Table:- Materials utilized in the fabrication of nanocomposite films made of CS-TiO<sub>2</sub> and PS/CS-TiO<sub>2</sub>**

Sr. No	Name of Chemical	Molecular weight (g/mole)	Density (g/cm <sup>3</sup> )	Purity	Manufacturer
1	Titanium isopropoxide (TTIP)	284.93	0.937	97%	Avara chemicals
2	Sodium hydroxide pellets (NaOH)	39.997	2.13	97%	S.D. Fine-Chemicals
3	Benzene (C <sub>6</sub> H <sub>6</sub> )	78.11	0.8765	99%	S.D. Fine-Chemicals
4	Acetic acid (CH <sub>3</sub> COOH)	60.052	1.05	99.9%	S.D. Fine-Chemicals
5	Polystyrene (CH <sub>2</sub> CH(C <sub>6</sub> H <sub>5</sub> )) <sub>n</sub>	-	1.04	Extra pure	HI-media
6	Chitosan (C <sub>6</sub> H <sub>11</sub> NO <sub>4</sub> ) <sub>n</sub>	-	-	Extra pure	HI-media

	H <sub>11</sub> N O <sub>4</sub> ) <sub>n</sub>				
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## CHARACTERIZATION

### Infrared (FTIR) Fourier Transform Spectroscopy

The FTIR spectra were recorded using an FTIR spectrophotometer (FTIR-8400, Shimadzu, Japan) with a resolution of 4 cm<sup>-1</sup> throughout the frequency, a scanning rate of 45, and a range of 400-4000 cm<sup>-1</sup> for the analysis of the functional groups of TiO<sub>2</sub>, chitosan, and CS-TiO<sub>2</sub>.

### Radiation Diffraction (XRD)

X-ray diffraction (XRD) was performed using a Model D8 Advance Bruker Limited Germany machine using XRD monochromatic Cu K $\alpha$  radiation (1.5406) at 40 kV and 40 mA in order to investigate the crystalline structures of TiO<sub>2</sub>NPs, CS-TiO<sub>2</sub>NPs, and PS/CS-TiO<sub>2</sub> nanocomposite film. The optimization of diffraction patterns was carried out within the angular ranges of 5 and 80 at a scanning speed of 1 degree per second (2).

### Size And Surface Morphology Of The Particles

Hitachi High Technology Corporation Ltd, Japan utilized a FESEM S-4800 Type II to take photos of CS-TiO<sub>2</sub>NPs and PS/CS-TiO<sub>2</sub> nanocomposite film in order to investigate surface morphology. CS-TiO<sub>2</sub>NPs were first dissolved in distilled water before the particle size was measured with a Malvern ZS-200 particle size analyzer from Worcestershire in the United Kingdom.

### Effect of Process Optimized Cu-Decorated-Rgo Nanocomposite on Deactivation of Food Born Pathogenic Bacteria

There is a correlation between consuming certain foods and contracting foodborne

infections such as *E. coli* and *S. aureus*. Both of these bacteria are responsible for the most rapid breakdown of protein-rich meals, including milk and other dairy products, meat, poultry, and shellfish. *E. coli* has the potential to thrive and create gas when the temperature is 45.5 degrees Celsius and the medium contains lactose. It will first establish a colony, and then it will generate a poison that will make humans sick. In food, heat-stable toxins that cause poisoning are produced by bacteria known as *S. aureus*.

The use of chemical preservatives poses a risk to human health. In order to prevent potentially harmful bacteria from growing and spreading in food or in the environment where food is prepared, an antibacterial agent is necessary. The use of inorganic antibacterial compounds, as opposed to organic antibacterial agents, is recommended for improving the stability and safety of the process. By applying inorganic antibacterial compounds in food packaging, it is possible to drastically cut down on the development of germs, which in turn will improve the shelf life of the food.

### CONCLUSION

Producing a food packaging film using Cu-decorated-rGO in LDPE at a weight percentage of 5% allowed for the production of a film with dramatically improved antibacterial properties. The tensile strength of the newly formed film increased by fifty percent in comparison to the undeveloped LDPE film, but the film's elongation at break decreased by five percent. The undeveloped LDPE film had a melting temperature that was 7 degrees Celsius lower than the temperature at which the produced film melted.

The WVP of the newly produced film was sixty percent lower than that of the LDPE film that had not yet been developed. At room temperature, the quantity of metal ions released from the film when acidic food was present was thirty percent more than when neutral food was present. As compared to room temperature, the generated film released a greater quantity of metal ions after being heated to 60 degrees Celsius for four hours (80 g/L for chilli vinegar and 50 g/L, respectively, for packed water).

As a result, it was shown that the release of metal ions from the film that was formed takes place in a manner that is dependent on both pH and temperature. During the antimicrobial test, the sample of peda that was packaged in developed film had its shelf life improved by 15 days, making it more suitable for storage. Because of these enhancements, it is now possible to utilize the Cu-decorated-rGO/LDPE film to prevent bacterial spoilage in food packaging. This is important since bacteria may cause food to spoil.

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