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THE SYNTHESIS of CAFESTOL LOADED ZnO NANOPARTICLES and THEIR CHARACTERIZATION

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EGE ÜNİVERSİTESİ FEN BİLİMLERİ ENSTİTÜSÜ

ETİK KURALLARA UYGUNLUK BEYANI

EÜ Lisansüstü Eğitim ve Öğretim Yönetmeliğinin ilgili hükümleri uyarınca Yüksek Lisans Tezi olarak sunduğum "The Synthesis of Cafestol loaded ZnO Nanoparticles and Their Characterization" başlıklı bu tezin kendi çalışmam olduğunu, sunduğum tüm sonuç, doküman, bilgi ve belgeleri bizzat ve bu tez çalışması kapsamında elde ettiğimi, bu tez çalışmasıyla elde edilmeyen bütün bilgi ve yorumlara atıf yaptığımı ve bunları kaynaklar listesinde usulüne uygun olarak verdiğimi, tez çalışması ve yazımı sırasında patent ve telif haklarını ihlal edici bir davranışımın olmadığını, bu tezin herhangi bir bölümünü bu üniversite veya diğer bir üniversitede başka bir tez çalışması içinde sunmadığımı, bu tezin planlanmasından yazımına kadar bütün safhalarda bilimsel etik kurallarına uygun olarak davrandığımı ve aksinin ortaya çıkması durumunda her türlü yasal sonucu kabul edeceğimi beyan ederim.

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Gülşah BALLICA

ÖZET

KAFESTOL YÜKLÜ ZnO NANOPARTİKÜLLERİNİN SENTEZLENMESİ ve KARAKTERİZASYONU

BALLICA, Gülşah

Yüksek Lisans Tezi, Kimya Anabilim Dalı

Tez Danışmanı: Doç. Dr. Yeliz YILDIRIM

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Çinko metali canlı metabolizması için oldukça önem arz eden nadir elementlerden bir tanesidir. Antibakteriyel, antimikrobiyal ve antikanser gibi özellikleri nedeniyle birçok araştırma grubu tarafından yoğun olarak çalışılmaktadır. Kafestol kahve yapısında bulunan antimikrobiyal ve antikanser özellikleri olan diterpendir.

Bu tez çalışmasında antimikrobiyal aktiviteye sahip Kafestol-Kitosan-ZnO nanopartikül sisteminin sentezlenmesi amaçlanmaktadır. Bu amaçla, çinko oksit (ZnO) nanopartiküllerinin istenilen boyutta sentezlenmesi için reaksiyon koşullarının optimizasyon çalışmaları, sentezlenen nanopartiküllere kitosan kaplanması ve kafestol molekülünün bağlanması yapılmıştır. ZnO nanopartikülleri kimyasal çöktürme metodu ile gerçekleştirilen optimizasyon çalışmaları sonucunda 45-60 nm boyut aralığında sentezlenmiştir. Sentezlenen ZnO nanopartikülleri kitosan doğal polimeri ile kaplanması sonrasında antimikrobiyal aktiviteye sahip kafestol molekülü bağlanmıştır. Çalışma esnasında moleküllerin kimyasal yapı analizleri Fourier Transform Infrared (FTIR) cihazıyla, boyut analizleri Malvern Zeta Sizer ve Scanning Electron Microscope (SEM) yöntemleriyle, termal özelllikleri Thermogravimeti Analysis (TG) ve Differential Scanning Calorimeter (DSC) cihazlarıyla incelenmiştir.

Anahtar sözcükler: ZnO, nanopartikül, kitosan, kimyasal çöktürme, kafestol.

ABSTRACT

THE SYNTHESIS of CAFESTOL LOADED ZnO NANOPARTICLES and THEIR CHARACTERIZATION

BALLICA, Gülşah

MSc in Chemistry

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Zinc metal is one of the rare elements, which is very important for the metabolism of the human. Due to its properties such as antibacterial, antimicrobial and anticancer, many research groups are working intensively. Cafestol is a diterpene with antimicrobial and anticancer properties.

In this thesis, it is aimed to synthesize the Cafestol-CS-ZnO nanoparticle system which has antimicrobial activity. For this purpose, the optimization of reaction conditions for the synthesis of zinc oxide (ZnO) nanoparticles in the desired size, chitosan coating of the synthesized nanoparticles and binding of the cafestol molecule were performed. ZnO nanoparticles were synthesized in 45-60 nm size range as a result of optimization studies with chemical precipitation method. After synthesized ZnO nanoparticles with chitosan natural polymer, the cafestol molecule with antimicrobial activity was bound. During the study, chemical structure analyzes of the molecules were investigated with Fourier Transform Infrared (FTIR), size analyzes were performed by Malvern Zeta Sizer and Scanning Electron Microscope (SEM) methods and their thermal properties were examined with Thermogravimetry Analysis (TG) and Differential Scanning Calorimeter (DSC) devices.

Key words: ZnO, nanoparticle, chitosan, chemical precipitation, cafestol.

ÖNSÖZ

Günümüzde Nanoteknolojiye artan ilgiyle birlikte yeni bir kavram olan "nanopartiküller" oldukça yaygın kullanılmaya başlamıştır. Değişik materyaller elde ederek özellikle insan sağlığı için yararlı sistemler oluşturulmaya çalışılmaktadır.

Çinko, insan vücudunda bulunan önemli bir iz elementtir. Fazlası kadar yokluğunun da zararlı olduğu çinko, literatürde birçok araştırmanın çıkış noktası olarak yer almaktadır. Çinko sahip olduğu antimikrobiyal, antibakteriyel ve antikanser gibi özellikler bakımından oldukça zengin olduğu için ilgimi çekmiş ve güncel bir konu olan nanopartikül kavramıyla birlikte kullanıldığında sahip olduğu özelliklerin artması bakımından tez konumu belirlememde yardımcı olmuştur.

Zaman içerisinde insanın doğaya dönmesiyle doğal kaynaklardan nasıl yararlanacağı literatürde araştırma konusu olup, doğal bir polimer olan kitosan ve doğal bir kaynak olan kahveden elde edilen kafestol bu çalışmalarda yer alan malzemelerden bir kaçıdır. Kitosan ve kafestole baktığımızda ikisinin de antibakteriyel özelliğe sahip olduğu görülmektedir.

Çinko, kitosan ve kafestolün birlikte kullanıldığı bu tez çalışmasında boyut, yapı ve termal özellikleri inceledim.

İZMİR

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ABBREVIATIONS INDEX

DNA	Deoxyribonucleic Acid
AFM	Atomic Force Microscope
ZnO NP	Zinc oxide Nanoparticle
CS-ZnO NP	Chitosan-Zinc oxide Nanoparticle
Cafestol-CS-ZnO NP	Cafestol- Chitosan-Zinc oxide Nanoparticle
ROS	Reactive Oxygen Species
UV	Ultraviolet
CS	Chitosan
SEM	Scanning Electron Microscope
DSC	Differential Scanning Calorimeter
FTIR	Fourier Transform Infrared
TG	Thermogravimetry Analysis
T_{max}	The maximum weight loss temperature

1. INTRODUCTION

As a result of the technological research with low cost and multi-product opinion, the nanotechnology that emerged in 1959 started to attract great attention with the increasing population. The need for raw materials and resources began to emerge as a result of developing industrialization. Desired features are provided, by changing the dimensions of materials with nanotechnology (Villaverde, 2010).

The increase interest in nanotechnology has led to an increase in the usage area. Nanotechnology, especially in the medical and biomedical field, is important to improve the quality of human health. In some studies, some cancer drugs have been found to be ineffective due to the resistance of the tumor to these drugs. In the study, it was observed that the drug given by Paclitaxel nanoparticles exceeded the brain barrier, overcome the resistance, and the drug acted on the brain cancer cells (Koizara et al., 2004).

Due to the deterioration of bronze and copper implants used for human health in history and the erosion of metal prostheses, studies have been carried out and the properties of these materials have been altered and their damage has been eliminated (Gümüşdereli, 2002).

Various terms (nanocrystals, nanoparticle, nanotubes, etc.) have emerged with nanotechnology. Nanoparticles, one of these terms, are highly preferred materials with a size less than 100 nm. The nanosize of the materials is of great importance in terms of both physical and chemical properties. The changing properties of nano materials vary in their application areas. Nanoparticles are classified as polymeric and metallic according to the usage areas. Polymeric nanoparticles are especially used in drug delivery systems with synthesized biocompatible polymers. Preferred reasons for these nanoparticles are; easy sterilization, deterioration in physiological conditions, non-toxic and high active substance loading capacity (Derman et al., 2013).

Metallic nanoparticles are generally synthesized in the form of metal oxides. The size and surface properties of metal oxide nanoparticles increase their use over normal size metal oxides. To improve biosensor performance, Au nanoparticles were immobilized on the Silane-modified surface, resulting in improved biosensor performance with bonds between Au nanoparticles and enzymes (Kerman et al., 2008).

Metal oxide nanoparticles with antimicrobial properties are prominent in the medical field. The metal ion in the nanoparticle provides a positive charge, binds to the negative surface in the bacteria and causes cell death as a barrier to the inhalation of the bacterial cell (Seil and Webster, 2012).

Zinc is a trace element that needs to be taken 20 mg daily and is present in the structure of at least one enzyme in the living body (Fierke, 2000). Since zinc plays a role in many events in human metabolism, many diseases are seen due to zinc deficiency in metabolism. Growth retardation (Arcasoy, 2002), visual impairment (Tate et al., 2002), diarrhea (Blanchard, 2000), sensorial disorders (Sato and Kondah, 2002), cancer (Costello et al., 1999) and heart disorders (Rostan et al., 2002) are seen in zinc deficiency.

Nanoparticle structures in the form of zinc oxide provide many physical and chemical advantages. Zinc oxide nanoparticles are distinguished from other metal oxides due to their biocompatibility and low toxicity. Zinc oxide nanoparticles have different properties. Anticancer properties of zinc oxide nanoparticles; The synthesized zinc oxide nanoparticles in the presence of mercaptopropionic acid , it has been proven in studies conducted on breast cancer cells as a result of the binding of curcumin to nanoparticles (Ghaffari et al., 2017). Antidiabetic properties of zinc oxide nanoparticles; as a result of ZnO nanoparticles given to diabetic rats at different doses, it was observed that these nanoparticles were strong diabetic agents when glucose and insulin levels were measured (Nazarizadeh and Asri-Rezai, 2015). The effects of zinc oxide nanoparticles experiment against Pseudomonas aeruginosa bacteria were evaluated in vivo and it was observed that zinc oxide nanoparticles had antibacterial properties (Dwivedi et al., 2014). Considering to antifungal properties of zinc oxide nanoparticles, the studies on Candida albicans, a pathogenic yeast, showed inhibition of these yeasts due to the concentration of zinc oxide nanoparticles (Lipovsky et al., 2011).

Biodegradable polymers that are insoluble in water and subject to changes in physical and chemical properties with biological fluids are important today. Chitosan, a biodegradable polymer, is produced from natural sources and is non-toxic. Chitosan is attracting attention in many fields of industry due to its functional groups such as amine, hydroxyl (Lee et al., 2004). Chitosan is used in the treatment of wound. The effect of chitosan on the wound was tested in wounds created in rats and chitosan had a positive effect on wound healing process (Cho et al., 1999).

Complementary treatment favors the scientific medicine methods. Alternative treatment is the treatment that cannot be scientifically proven (Tuncer, 2014). In alternative treatment, it is believed that plants and natural resources are beneficial and healing effects. Studies are continuing to show that antioxidant plants are effective in treating cancer (World Health Organization, 2018).

The coffee, which is among the most consumed beverages in the world, consists of many components. Coffee contains purine derivatives, chlorogenic acid derivatives and specific diterpenes such as cafestol, kahweol (IARC, 1991). Cafestol, one of the components of coffee, exhibits anticancer and anti-inflammatory properties (Cavin et al., 2002). In a study using cafestol, apoptosis was induced in renal carcinoma lines (Choi et al., 2011). The antioxidant effect of cafestol was investigated and a smaller amount of intracellular ROS (Reactive Oxygen Species) was observed in cells exposed to H_2O_2 when treated with cafestol (Lee and Jeong, 2007). This feature of cafestol is of great importance because the risk of cancer cells increases as the amount of ROS increases. The properties of cafestol are still being investigated with current studies.

The aim of this thesis is to synthesize the CS-ZnO nanoparticles loaded with cafestol and to make characterization studies of the synthesized structure.

2. GENERAL INFORMATION

2.1. Nanotechnology

When the measurement accuracy and development of technology were examined, the process that started with the mechanical age, as the sensitivity increased, went into the electronic age(10^{-4}-10^{-9} m) and then to the nano age(10^{-9}-10^{-12} m) (Erkoç, 2014). The interest in technology is increasing day by day from the perspective of developing societies. In order to define the nanometer (nm) size, it can be considered that an ant is in the size of one million nanometers and that the blood cells are thousands of nanometers and that the deoxyribonucleic acid (DNA) molecules we know are in the nanometer size. The word nano originates from the Greek word “nanos” and means “dwarf”. The sizes of the nanostructures are usually between 10-100 nm. In 1959, Richard Feynman’s speech term “nanotechnology” came from with the title “There’s Plenty of Room at the Bottom”. According to Feynman, it was possible to see atoms, reduce computers and treat patients with robotic pills. Only 27 years after Feynman’s speech, atoms could be visualized with an atomic force microscope (AFM) (Caltech, 1960).

In 1993, the first nanotechnology laboratory was established in the US, and studies for the materials in nanoscale were accelerated. The positive results of the studies have been observed and a significant amount of budget has been allocated in the US in 2000 for nanotechnology research. In 2001, a short time after the ZnO nanowire laser was made, nanotechnology came into prominence with the construction of nanocars in 2005 (Shirai et al., 2005).

Thanks to nanotechnology, the size of the materials can be reduced and the electronic devices can be developed faster. The chemical and physical properties of the materials have been changed, durable and easy-to-use versatile materials have been started to be made. As a simple example, it was found that when the gold element was normal size, it could not interact with the materials, on the other hand, nano-scale gold type particles interacted easily with this materials (Villaverde and Rodriguez-Carmona, 2010).

2.1.1. Nanotechnology and Usage Areas

The use of nanotechnology with the developing industry has expanded. Some of these areas of use are medical applications, pharmaceuticals, textiles, food industry and electronic-automotive fields. When the applications of nanotechnology in medicine are examined, the concept of “nanomedicine” has emerged with the use of nanotechnology. As a result of nanomedicine studies, achievements were obtained for cancer treatment (Song et al., 2017), AIDS treatment (Liu and Chen, 2016), nuclear medicine (Drude et al., 2017) and many other diseases.

Feynman’s (Caltech, 1960) patient-robot situation, which he said was possible in his speech in 1959, was produced by researchers and a two-armed nanorobot was produced. This robot is placed in DNA origami to form the desired DNA using its arms as a weapon. (Gu et al., 2010; Gu et al., 2009). Another use of nanotechnology in the medical field is the prevention of deterioration of the drug molecule to be transported using nanoparticles, regulation of this drug molecule, and regulation of drug retention in drug delivery. Due to their advanced properties, they can withstand physiological stress and pass through the blood brain barrier to ensure proper distribution (Suri et al., 2007). The use of nanotechnology in drug delivery systems is a preferred method for preventing side effects caused by the spread of medicines used for therapeutic purpose. In the literature, since the use of catheters for non-invasive bladder cancer is not a comfortable method for the patient and the bladder has the desire to ejaculate for two hours, it was seen that the drug was excreted. The drug delivered with biodegradable nanoparticles reached the desired site and controlled release was performed. In this way, it was seen that there was no need to use a catheter and the patient began to take the drug under appropriate conditions (Bilensoy vd., 2015).

Nanoparticles have been introduced into cosmetic field. The most undesirable situation in the cosmetic industry is the lack of effective of the active substance, which provides the desired effect in the product. It is unwanted that most cosmetic products cannot penetrate the skin. To eliminate this condition, nanoparticles are ideal carriers and protect lipophilic cosmetic products (Turgut vd., 2011).

The developed nanostructured materials have also gained importance for biosensors over time. Biosensors developed, because of monitor the structures of healthy/sick conditions. The purpose of using nanostructured materials in this field is to change the properties such as electrochemical and optics, to observe the response-time movements of target biomolecules and to easily monitor drug toxicity (Kerman et al., 2008).

Nanotechnology offers new food and material for micro and nano-size of processing, product development and food safety. By using biotechnology, nanotechnology and information nanotechnology, nanobiosensors have been progressed recognize pathogens and contaminants for foods. Thanks to these nanobiosensors, aroma and flavors are detected electronically. Nanotechnology is used in food industry with antimicrobial properties for protecting food products (Chaudhry et al., 2008). World-renowned brands are making efforts to obtain products with nanotechnology that can change the color, aroma of drinks and the texture (Neethirajan and Jayas, 2011).

The relationship between agriculture and nanotechnology include pesticides, water treatment and soil cleaning areas. Nanosensors which are colored by binding to microorganisms, nanoporous filters to remove pathogens and contaminants and nanoparticles for catalysis and oxidation are used in this field (Süfer ve Karakaya, 2011).

The nanotechnology, which meets with the textile industry, has been developed with power ignition feature. Nanoparticles reinforced Nylon 6.6 fibers have been shown to increase the power ignition property (Doğan vd., 2005). In addition, nanoparticles are used in textile industry with their odor, antibacterial, antimicrobial, and antifungal properties and are of great importance for the controlled release of biocides (Ghosh, 2005).

2.2. Nanoparticles

Nanostructured materials can be composed of many different structures. These structured contain nanocrystals, nanoparticles, nanotubes, nanowires and nanofilms. The reasons for the difference in the structures are the size-volume properties (Goldstain, 1997). The nanoparticle opinion, expressed by nanotechnology, has different morphologies and is termed with similar shapes as core-shell, doped, spherical, metallic and polymeric.

Nanoparticles are usually less than 100 nm in size and these particles are building blocks of nanotechnology. Nanoparticles are highly preferred materials because their physical and chemical properties differ from normal size materials. These are electronic structure and surface-to-volume ratio (Liveri, 2006). Nanoparticles are widely used commercially in household applications, material coatings, biomedical applications, biosensors and similar fields.

The preparation of nanoparticles is generally done using the terms “Top Down” and “Bottom Up”. In addition to these approaches, these nanoparticles can be prepared by chemical vapor condensation method (for hydrogen and oxide nanoparticles), hydrogen reduction, inert gas condensation, production from micro hydrogen systems, flame synthesis, metallic etching, spray pyrolysis and chemical precipitation methods (Gürmen ve Ebin, 2008).

2.2.1. Synthesis Methods of Nanoparticles

The opinion of “Top Down” is the disintegration of the material to the nanoscale by mechanically or chemically energizing the volumetric material from the outside. Mechanical grinding and etching methods are referred to as “Top Down”.

The concept of “Bottom Up” is the formation of a nanosize structure from an atom or molecule using a chemical process. Chemical vapor coating-condensation, sol-gel and spray pyrolysis methods are referred to as “Bottom Up” (Gürmen ve Ebin, 2008).

The chemical vapor condensation (CVC) method was introduced in 1994 in Germany and used to produce large quantities of product. The most important feature of the CVC method is that it can be produced easily because it does not require a specific starting material (Wang et al., 2003). In generally, it is the thermal decomposition of the gaseous material using a carrier gas. The types of gas, flow and process temperature are important parameters for this method (Gürmen ve Ebin, 2008).

The hydrogen reduction method is important for Fe, Ni and Co nanoparticles. The method consists of particle formation, collection of particles formed and gas washing steps. The object is to move the starting material to the preheated zone with the aid of the carrier gas and then evaporate by moving it to a warmer area for particle formation (Jong et al., 2004). Reaction-zone temperatures and concentration of the starting material are important parameters for this method (Suh et al., 2006).

The inert gas condensation is the method found in 1984 to make nanoparticles directly in the over saturated vapor phase of metals and alloys. In the method, the heated water evaporates and begins to lose heat due to its interaction with the environment. At this time, when the droplets reach the over saturating, clumps of atoms are formed on the surface of the cold glass. These clusters and gas molecules in the system collide to form particles. The evaporation rate of the starting material, the reaction temperature and the type of gas are important parameters for the method (Roth, 2007).

In the synthesis method of microheterogen systems can be used liquid crystals, gels, micelle solutions and microemulsions. This method is fast and low cost. Nanoparticle synthesis can be performed for metal oxide, metal sulphate and water-insoluble materials. The method is simple and following the selection of the microheterogen, the synthesis is carried out by dissolving the starting material and allowing it to stir. This method is the most preferred method for nanoparticles with metallic and magnetic properties (Liveri, 2006).

Flame synthesis method is used for commercial production because of its low cost and size control. Since metal halides have easy volatility, they are preferred as starting material. In the method, after the starting material passes to the vapor phase, atomic clumps are formed by transporting this vapor to the flame medium with the carrier gas. Particles are obtained by combining the formed clusters (Roth, 2007).

The mechanical etching method was developed for the 1970s in industry area to obtain new alloy. After the grinding of the brittle materials the fine powders obtain. The high frequency and low amplitude vibrations are used to make the nanoparticle. In the method there are disadvantages such as oxidation of metals and impurities from nitrogen structures. To solve this problem, nitrogenous structures are eliminated by using invert gas using oxidized seals (Edelstein and Commorata, 2001).

Ultrasonic spray pyrolysis is a wide range of applications in the medical field. Thin films and powders can be produced using this method. In the method, the droplets are composed of the starting material as the aerosol and the thermal decompositions control the phase change. The droplet size, the properties of the starting material, the temperature and the duration are important parameters for this method (Tsai et al., 2004).

While nanoparticles can be synthesized by various synthesis methods, they can occur naturally by soil erosion, forest fires and volcanic eruptions (Tunca, 2015).

2.3. Metal Oxide Nanoparticles

The increase in nanotechnology has raised the diversity of nanoparticle species and increased interest in metallic nanoparticles. Metal oxide nanoparticles show indicating various properties such as energy storage, catalysis effect and semiconductor. Due to these properties, metal oxide nanoparticles have an important place especially in the fields of biomedical, industrial and water treatment (Zikalala et al., 2018).

The interest of metal oxide nanoparticles especially in the field of industry is due to their advanced optical, electrical and magnetic properties. The dimensions of metal oxide nanoparticles are very important for such mentioned above properties and physicochemical properties (Kim et al., 2018). As the surface area-volume ratio increases, the heat treatment, mass transfer, dissolution rate and catalytic activity of the particle increases (Buzea et al., 2007). Metal oxide nanoparticles are used for the mass production of stable colloidal solutions, especially in industry.

Another advantage of metal oxide nanoparticles is the facilitation of redox process forming the chemical bonds with enzymes. This property improves the biosensor performance of the metal oxide nanoparticles (Kerman et al., 2008).

As pathogens started to gain resistance against antibiotics, health problems were increased and treatment failures were observed due to this resistance condition. Nanotechnology has started to gain importance in biomedical field thanks to the antimicrobial properties of metals in nanoscale. More than 70% of bacterial infections are known to be resistant to antibiotics (Allahverdiyev et al., 2011). Treatment studies are carried out using silver (Ag), copper (Cu), gold (Au), titanium (Ti) and zinc (Zn) metals whose antimicrobial properties are known against this antibiotic resistance (Malarkodi et al., 2014). Antimicrobial properties of metal oxide nanoparticles (CuO, Ag_2O, TiO_2, ZnO etc.) were investigated by different research groups. In vitro studies of these metal oxide nanoparticles have shown that microbial species are inhibited (Dizaj et al., 2014). The antimicrobial properties of metal oxide nanoparticles vary according to the type and size of the nanoparticles. There are two reasons why the metal oxide nanoparticles have antimicrobial properties. These reasons; toxicity of free metal ions formed in the environment by dissolving metals from the surface of nanoparticles and oxidative stress in the environment provide antimicrobial properties. (Besinis et al., 2012). The positive surface load of the metal nanoparticle results in the death of the bacteria by binding to the negative surface in the bacteria (Seil and Webster, 2012).

Metal oxide nanoparticles can be synthesized by physical and chemical methods. Physical methods include spray pyrolysis, ultra sonication and chemical evaporation. However, physical methods have limitations as they provide a uniform particle size for metal oxide nanoparticles and require a high cost device. In chemical methods, the metal oxide nanoparticles can be obtained by oxidation-reduction or by precipitation of the metal ion in the aqueous medium. Although chemical method contributes to the synthesis of metal oxide nanoparticles having various morphologies, it has harm to the environment and human health due to the toxic chemicals used (Zikalala et al., 2018). In the chemical method, smaller dimensions are obtained compared to the physical method.

Chemical precipitation method, which is a method of chemical synthesis, is used for the synthesis of metal oxide nanoparticles in simple, inexpensive and low temperatures. Metal oxide nanoparticles of different sizes can be synthesized by parameters such as the type and concentration of the starting material, concentration of the reducing material, reaction time and temperature (Sheini, 2012).

2.4. Zinc

Zinc was considered to be element in the 1500s in history, but it was not considered as important until 1869. In study of Raulin's (Yıldırım, 2003), zinc was found to be the main source of necessity for living things. Zinc is found to be useful for biological systems with the ability of participation and also easily changeable ligands (Williams, 1989). Since there is no redox property of zinc, the risk of oxidant damage doesn't seen. Zinc is used as a basic component for almost every enzyme, as used in the catalytic domain (Fierke, 2000). Zinc atoms have an important place in many proteins except enzymes. The zinc finger motif is a frequent repetitive motif in transcription proteins (Berg and Shi, 1996). These fingers, which are important for the binding of DNA, use the single zinc atom in their structure for configuration. Places opposite the zinc atom initiate the transcription request and gene expression according to the state of the regions. The intracellular regulatory ion effect of zinc has become more important especially in today. One of the reasons for this importance is that the zinc is easily recyclable for cross-linking (Hambidge, 2000).

Zinc is important for human nutrition. Defects in metabolic functions were observed due to zinc deficiency (Williams, 1989). Considering the importance of zinc for cell growth and differentiation, the sensitivities based on zinc deficiency are observed (Chesters, 1982). In the 1950s, zinc was accepted as a basic micronutrient for humans and abnormalities due to zinc deficiency were observed. Considering the heavy zinc deficiency, a lot of information about the biology of zinc has been obtained as a result of the researches carried out from past to present and it has been observed that the metabolic functions caused by zinc deficiency have been observed for all tissues and organs. In some cases, the effects of zinc deficiency are difficult to distinguish from secondary protein energy deficiency. However, there was an increase in the rate of recovery after addition of zinc to the immune system. In another case, when the treatment of zinc for the central nervous system was initiated, motivation, alertness and sensitivity increased, and the same level of irritability and restlessness decreased (Walravens et al., 1978).

Considering a slight of zinc deficiency, which causes less severe effects besides the effects of heavy zinc deficiency, is important in terms of public health. It has been observed that follow-up of the zinc content in plasma is of great importance for children sensitive to diarrhea (Bahl et al., 1998). With this control and subsequent treatment of zinc supplements, mild zinc deficiency can be treated and prevented. The amount of zinc in the gut decreases during the diarrhea process. This causes impairments for the immune system and mucosal cell transport (Ghishan, 1984). Zinc used in treatment decreased diarrhea time (Bhutta et al., 1999).

When the human body is examined, it is seen that the highest amount of zinc in males accumulates in prostate gland. Zinc and citrate have an important place for prostate. This is because zinc inhibits the oxidation of the mitochondal (m-) acconitase citrate to the isocyrate, which plays a role in catalysis in the first step of the cycle, taking place in the Krebs cycle. Because of this condition, the citrate accumulates in the prostate and the prostate fluid is secreted. This effect of zinc is valid for all mammalian cells, but is more important in prostate cells. Since this inhibitory effect is decreasing the amount of zinc, the energy source of the Krebs cycle decreases and causes the death of aerobic cells. This damage results in the growth effect of prostatic cancer cells (Singh et al., 2006). For prostate cancer, zinc appears to have an important role in preventing the spread of cancer cells.

2.5. Zinc Oxide Nanoparticles: ZnO NPs

ZnO NPs having a size of less than 100 nm have opaque properties against UV light, transparency against visible light. Thanks to this feature, ZnO NPs are used in sun creams (Ubani and Ibrahim, 2019). ZnO nanostructures morphologically can be found in structures such as nanoparticle, nanowire, nanofilm, nanorod and nanoring (Peng and Qin, 2011).

The most important properties of ZnO NPs for biomedical and medical fields are anticancer and antimicrobial properties. These properties are due to ROS formation. According to other metal oxide nanoparticles, ZnO NPs are biocompatible and have low toxicity. The effect of ZnO NPs as anticancer, antidiabetic, antibacterial and anti-inflammatory agents was investigated in many studies.

2.5.1. Research on ZnO NPs

ZnO NPs have anticancer properties because they induce ROS production and apoptosis. Due to the electrostatic properties of ZnO NPs, neutral hydroxyl groups are absorbed on their surfaces and this causes the surface charge change. Protons move from the surface of the particles with the high pH in the aqueous medium to ensure that the ZnO NPs have a negatively charged surface area and ZnO^- structures are formed. If this happens at low pHs, the protons that come to the environment will accumulate on the particle surface to ensure that ZnO NPs have positive charge and $ZnOH_2^+$ structures are formed (Rasmussen et al., 2010; Qu and Morais, 2001). ZnO NPs have positive surface charges in physiological conditions, which is unfavorable for cancer cells with negative membrane potentials. At the time of interaction, the cellular uptake of nanoparticles causes electrostatic interactions that give rise to phagocytosis and cytotoxicity (Rasmussen et al., 2010).

ZnO's bandwidth and semiconductor feature produce reactive oxygen species (ROS) and kill cells and give a natural photo luminance. In studies with culture cells, ZnO nanosheet focuses on entering the culture cells and this condition has been demonstrated by the yellow-orange light emission of cells in ultraviolet (UV) (Jiang et al., 2011).

ZnO NPs have been studied for diabetes activity due to play of important role into insulin metabolism such as synthesis, storage and secretion. In one of these studies the differences of, ZnO NP and $ZnSO_4$ were interpreted by working with rats. ZnO NPs have been observed to have more antidiabetic effect than $ZnSO_4$ when the high glucose and insulin levels are examined (Nazarizadeh and Asri-Rezaie, 2015).

The antibacterial properties of ZnO NPs come from their ability to induce oxidative stress due to their structure. Zn^+ ions released in the ZnO compound combine with the thiol group of respiratory enzymes. Bacteria are absorbed in the Zn^+ ion compared to ZnO NPs and bind to respiratory enzymes to reduce the effect of the enzyme. Free radicals in the environment by creating ROS multiply and consequently cause oxidative stress. ROS irreversibly damage the bacteria of membranes, DNA and mitochondria and bacterial cell die (Dwivedi et al., 2014).

ZnO NPs, which are antibacterial, also exhibit antifungal properties. The effects of ZnO NPs on a fungal species were investigated by some research groups. ZnO NPs with a concentration of 0,1mg/ml were found to inhibit 95% of the fungal species. ZnO NPs were also shown to increase the mortality rate in visible light (Lipovsky et al., 2011).

In other study, it was observed that ZnO NPs were able to penetrate into the deeper layers of the skin. ZnO NPs can also be effective against local skin inflammation (Ilves et al., 2014).

In addition to their antimicrobial properties, ZnO NPs are stimulating for the healing of the injured surface by the proliferation of epithelial cells. High concentration may be fatal for cells, while low concentration ZnO NPs are prominent for their healing effect. In the studies on this feature, the biodegradable polymer in hydrogel form with chitosan and ZnO NPs create composite bandages. With these bandages applied to wounds in rats, epithelial tissue formation with rapid epithelial cell proliferation and wound healing increased (Kumar et al., 2012).

2.6. Biodegradable polymer: Chitosan

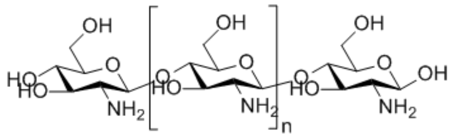

Figure 2.6 Chitosan

The material to be used in living tissues needs to adapt to the changing conditions within the body. Materials to be used as tissue engineering or drug delivery system in the body should be biocompatible. The term biocompatibility means that it is capable of responding appropriately to the living body system when applied. These materials are divided into four groups: metals, ceramics, polymers and composites. Biopolymers are the most commonly used biomaterials on living things. Chitosan is one of the most prominent polymers in the family of biopolymers.

Chitosan (Figure 2.6), which is obtainable from natural sources, considerable, eco-friendly, in terms of biodegradability and biocompatibility highly preferred are biopolymers. Chitosan are separated from other biodegradable polymers with physical and chemical properties. Chitosan dissolves well with dilute acid solutions (pH<7) while it is insoluble in water. The reason for not dissolving chitosan in pH>7 medium is due to its stable structure (Tuncer, 2014).

When the chitosan is dissolved, the amine group in the structure of the chitosan has a positive charge by protonating. With this feature, chitosan can be characterized as cationic polysaccharide (Lee et al., 2004). Chitosan can interact with negatively charged polymers, macromolecules and polyanions with its cationic properties.

Chitosan is a highly preferred biopolymer in the industrial field due to its acid removal, antitumor, antioxidant and antibacterial properties. Chitosan is generally used for coagulation and flocculation in water treatment, for plant additive and antimicrobial substances in agriculture, for enzyme immobilization in biotechnology, for additives in the food industry, for wound treatment in the medical field, for drug release and hydrogels (Demir ve Seventekin, 2009).

Chitosan has an important role in wound treatment. It has been tested in the wounds of rabbits and the healing rate of these wounds has been reported (Cho et al., 1999). Using chitosan in wound treatment, “chitosan wound bands” have been produced. These bands have been used in the Iraq war and have been found to play an active role in the cessation of blood and subsequent wound healing (Shahidi et al., 1999).

In vivo studies have shown that chitosan does not harm the human body and is degraded by lipase enzymes when used as tablets. After the structural degradation of chitosan by lipase enzymes, the formation of amine sugars in the environment and these sugars are not toxic. (Demir ve Seventekin, 2009).

2.7. Cafestol

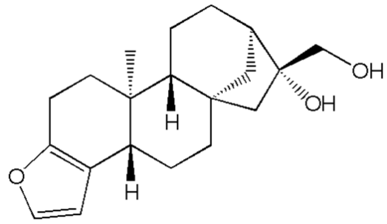

Figure 2.7 Cafestol

Nowadays, besides many scientific treatment methods, complementary treatment methods are shown to support these scientific methods. Alternative treatment methods are the treatment methods that are outside of these scientific methods and whose effects cannot be proven scientifically. In alternative therapy, it is believed that plants and natural resources are beneficial and have effects during the healing process. Studies on these fields are still in progress (World Health Organization, 2018).

Coffee has different bioactive compounds, including chlorogenic acid and purine derivatives, specific diterpenes such as cafestol, kahweol (IARC, 1991).

It is observed that cafestol (Figure 2.7) is used as a new natural compound in cancer studies. Heterocyclic aromatic amines in the colon tissue in animals are cancer risk factors. In studies conducted on this, it was observed that the cafestol and kahweol prevented the formation of heterocyclic aromatic amines in the colon tissue and decreased the amount of these structures (Huber et al., 1997).

The antioxidant effect of cafestol was investigated by Lee and Jeong. It was shown that when cafestol was treated on cells exposed to H_2O_2, the amount of ROS was decrease in intracellular (Lee and Jeong, 2007). This feature of cafestol is of great importance because the risk of cancer cells increases as the amount of ROS increases.

3. EXPERIMENTAL

3.1. Material

Zinc(II)sulfatheptahydrate [$Zn(SO_4).7H_2O$, Merck], sodium hydroxide [NaOH, VWR], chitosan [CS, Sigma], acetic acid [CH_3COOH, 100%, sigma] and cafestol were used.

In the characterization studies of ZnO nanoparticles, particle sizes were determined by using Malvern Zetasizer nano ZS device. Particles were characterized by using Perkin-Elmer Diamond Thermogravimetry Analysis (TG), TA Instruments Q20 Differential Scanning Calorimeter (DSC), JEOL JSM-7100F Branded Scanning Electron Microscope (SEM), Perkin-Elmer Spectrum 100 Fourier Transform Infrared (FTIR) analysis methods.

3.2. Synthesis and Characterization of ZnO Nanoparticles

The solutions of 0,2 M zinc salt and 0,4 M NaOH were prepared. They were mixture as 1:2 ($Zn(SO_4)_{(aq)}$,$NaOH_{(aq)}$) molar ratio by dropwise. Stirring was continued for 18 hours and the resulting white zinc hydroxide precipitate was filtered with filter paper. To remove residual chemicals, the resulting precipitate was washed with purified water and dried in an oven. For ZnO nanoparticles calcined at 400°C (Mohan and B, 2015). The reaction conditions (zinc salt type, salt concentration, base type, stirring rate, calcination time and mixing time) were optimized to ensure that the size of the ZnO nanoparticle was 45-60 nm.

3.2.1. Optimization studies

For the synthesis of the desired size ZnO NPs, the method of section 3.2 was used. Type of zinc salt in the method ($ZnCl_2$, Zn (SO_4)), salt concentration (0.04; 0.1; 0.2; 0.5 M), base type (NH_3, NaOH), reaction time (6, 12, 18 , 24 h), mixing speed (300, 400, 500 rpm) and calcination time (1, 2, 3 h) parameters were determined to obtain the desired size.

3.3. Synthesis of ZnONP-CS

0,4% chitosan was prepared by mixing with acetic acid for 24 hours. Chitosan (CS) solution was added dropwise over ZnO NPs dispersed in acetic acid and stirring for 24 hours.

3.4. Synthesis of ZnONP-CS-Cafestol

5 ml of 10mg/100ml of cafestol solution were added to the synthesized CS-ZnONP solution and stirring for 48 hours. At the end of the reaction, the solvent was removed and allowed to dry in a vacuum oven.

4. RESULTS and DISCUSSION

ZnO NPs were synthesized by chemical precipitation. The reaction mechanism in the method is as follows (Mohan and B, 2015):

$$Zn(SO_4).7H_2O+2NaOH \rightarrow Zn(OH)_2+Na_2(SO_4)+7H_2O$$

$$Zn(OH)_2+2H_2O \rightarrow [Zn(OH)_4]^{2-}+2H^+$$

$$[Zn(OH)_4]^{2-} \overset{\Delta}{\leftrightarrow} ZnO+H_2O+2OH^-$$

$Zn(OH)_2$ structures formed in the reaction affected the size of the nanoparticles and optimization studies were performed. The size-optimized ZnO NPs were coated with chitosan (CS-ZnO NPs) and then cafestol was ligated to CS-ZnO NPs.

4.1. Optimization of ZnO NPs

As a result of the optimization studies, the mean size measurements taken by DLS using Zeta Sizer are given in Table 4.1 (a, b, c, d, e, f) and Figure 4.1 (a, b, c, d, e, f). Based on these results, the optimization process was completed with ZnO NPs with an average size of 50 nm.

Zn Salt	Size (nm)
$Zn(SO_4)$	**188**
$ZnCl_2$	254

Table 4.1 a) Optimization of Zn salt type

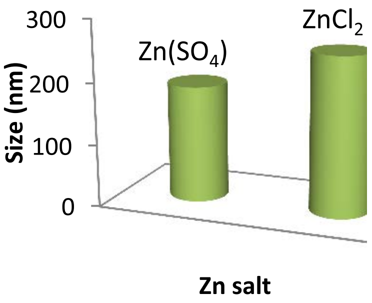

Figure 4.1 a) Optimization of Zn salt type

Concentration of Zn (M)	**Size (nm)**
0,04	2603
0,1	458,7
0,2	**188**
0,5	352,3

Table 4.1 b) Optimization of the concentration of Zn

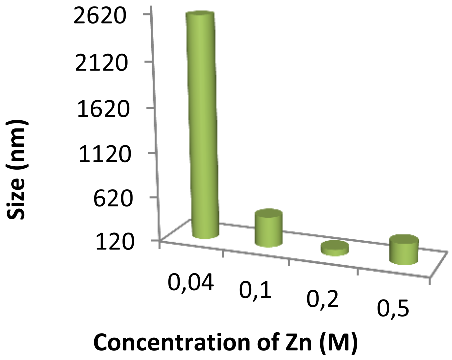

Figure 4.1 b) Optimization of the concentration of Zn

Base	**Size (nm)**
NH$_3$	325
NaOH	**188**

Table 4.1 c) Optimization of base type

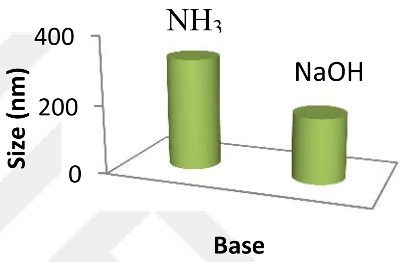

Figure 4.1 c) Optimization of base type

Reaction Time (h)	**Size (nm)**
6	Out of measurement accuracy
12	255
18	**188**
24	950

Table 4.1 d) Optimization of reaction time

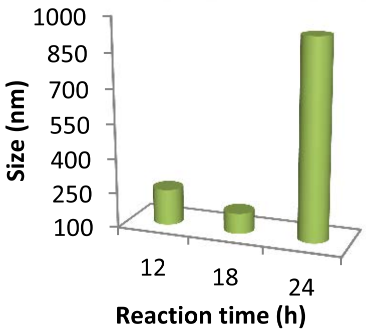

Figure 4.1 d) Optimization of reaction time

Mixing Speed (rpm)	**Size (nm)**
300	188
400	**50**
500	111

Table 4.1 e) Optimization of mixing speed

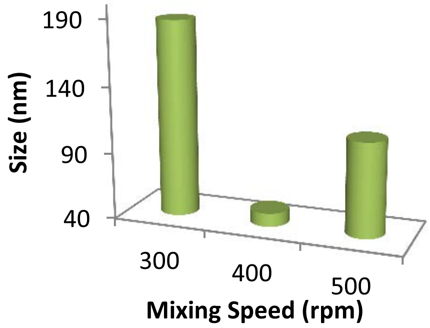

Figure 4.1 e) Optimization of mixing speed

Calcination Time (h)	Size (nm)
1	141,8
2	**50**
3	136,2

Table 4.1 f) Optimization of calcination time

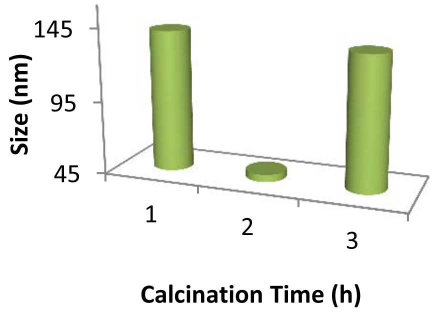

Figure 4.1 f) Optimization of calcination time

The optimal conditions for the preparation of ZnO NPs of the desired size are shown in Table 4.1 g).

Zn salt	Concentration of Zn (M)	Base type	Reaction time (h)	Mixing speed (rpm)	Calcination time (h)
$Zn(SO_4)$	0,2	NaOH	18	400	2

Table 4.1.g) Optimum conditions for the synthesis of ZnO NP

It was confirmed by the formation of Zn $(OH)_2$ structures in which the amount of base was important during the synthesis. It was observed that these structures affected the nanoparticle sizes. Due to its high surface area and energies, it was observed that ZnO NPs were agglomerated in some regions and large structures were formed.

4.2. Analysis of ZnO NPs

The FTIR spectrum of the ZnO NPs was obtained using the ATR technique. The peak at between 590-540 cm^{-1} in the spectrum is specific for ZnO (Janaki et al., 2015). OH peak is seen at between 3527-3134 cm^{-1} (Gnanasangeetha and Sarala Thambavani, 2013). The OH peak is due to the $Zn(OH)_2$ structures in the environment.

Surface images were taken using JEOL JSM-7100F Branded Scanning Electron Microscope (SEM). In order to increase the conductivity of the samples, a $8x10^{-1}$ mbar/Pa vacuum was applied on the Quorum coating device and a 10 mA voltage applied to gold-palladium (80-20%). The images were taken with 15 kV voltage applied. SEM analysis was performed based on the results obtained with DLS.

In the SEM images taken with different focus of the ZnO NPs synthesized (Figure 4.2 a-c) it was observed that the dimensions were in the 45-60 nm and they were morphologically spherical and hexagonal.

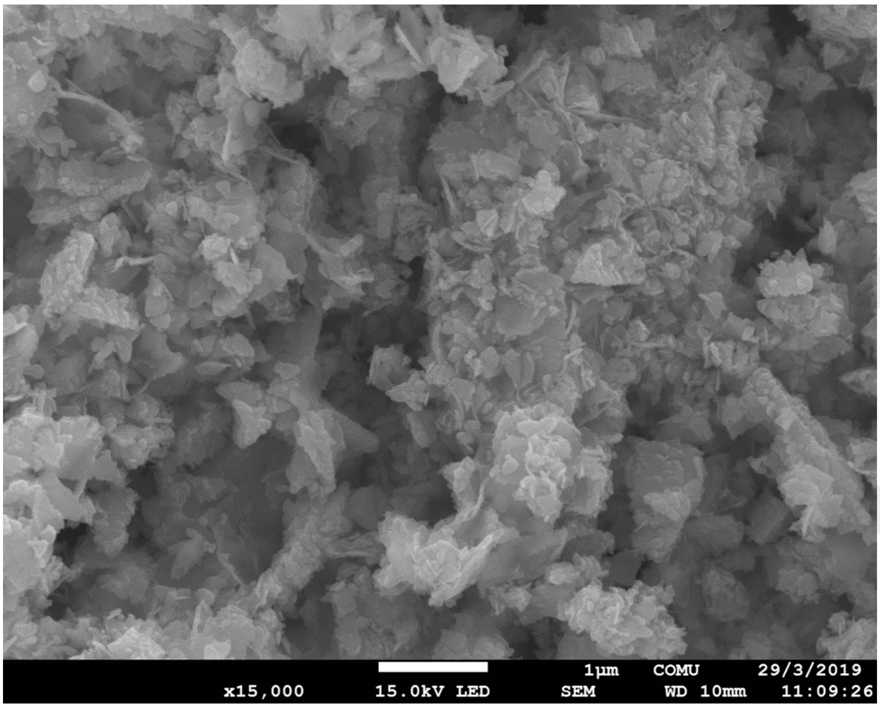

Figure 4.2 SEM image showing ZnO NPs a) x15000 Focused ZnO NPs

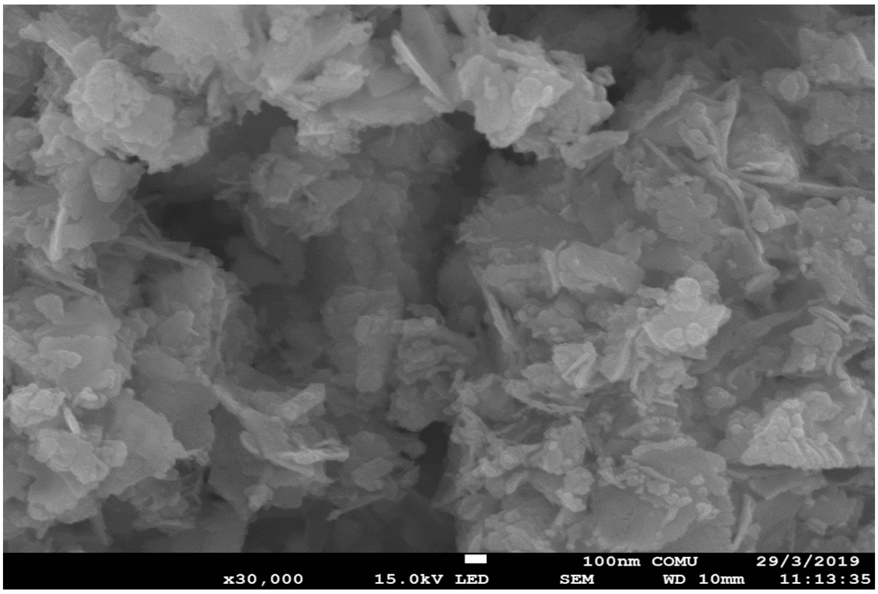

Figure 4.2 SEM image showing ZnO NPs b) x30000 Focused ZnO NPs

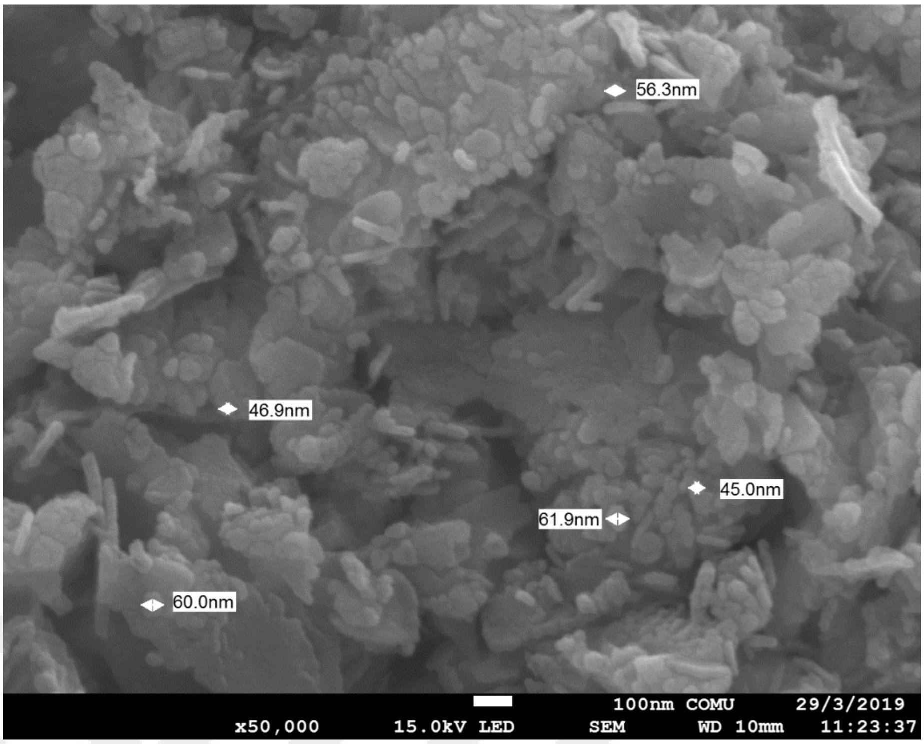

Figure 4.2 SEM image showing ZnO NPs c) x50000 Focused ZnO NPs

Xu et al. (2005), according to their study, SEM images of hexagonal structure ZnO nanoparticles were found to be 0.5 µm size. In the same study, it was observed that some of the particle structures were transformed into rods and their dimensions varied between 50-300 nm.

According to the study by Özbay and Gülce (2014), ZnO NPs with a hexagonal structure on the SEM images were found to be between 50-200 nm in size. In the study of Gnanasangeetha and SaralaThambavani (2013), in the literature, it was seen that they synthesized ZnO NPs by different methods and obtained SEM images of these nanoparticles with dimensions of 100-190 nm. Srivastava et al. (2013), ZnO NPs synthesized in the literature showed that the dimensions were in the range of 95-450 nm. The morphology of nanoparticles in images is mostly observed in rods, although they are hexagonal. In 2013, Kumar et al. synthesized ZnO NPs and measured their dimensions with SEM. They observed structures of different sizes in the range of 64-187 nm. Morphological differences were observed depending on the dimensions of the structures. When the SEM images of the ZnO NPs in the literature are examined, it is seen that the

SEM images obtained as a result of this thesis are compatible with the SEM images given in the literature.

TG measurement of ZnO NPs was obtained using a heating rate of 10°C/min in a nitrogen atmosphere in the range of 30 to 1000°C temperatures. When look at the thermogram in Figure 4.2 d), the first mass loss is observed at 0-100°C at 11%. This mass loss is the removal of the adsorbed water molecules and $Zn(OH)_2$ structures from the ZnO NPs. In the structure 89% of the mass belongs to Zn. The obtained TG thermogram was found to be tremendously compatible with the literature (Koutu et al., 2018).

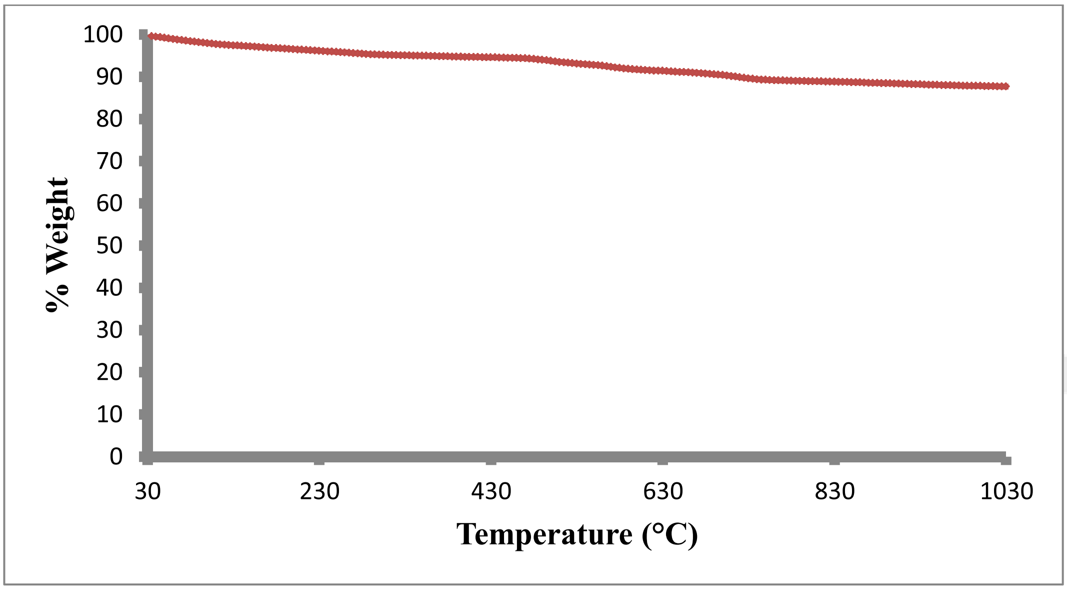

Figure 4.2 d) TG thermogram of the ZnO NPs

The synthesized ZnO NPs were analyzed by DSC. All DSC measurements were made by heating 10°C/min under nitrogen at 50ml/min. Looking at the Figure 4.2 e), small amounts of mass loss up to 85-95°C occurred and endothermic peak was formed. This shows that the structure of water and $Zn(OH)_2$ structures are deteriorated. An exothermic peak occurred in the range 292-317°C. The exothermic peak seen at 482-520°C is the peak resulting from the crystallization of ZnO. The peak values in the graph correspond directly to the literature (Tseng et al., 2012).

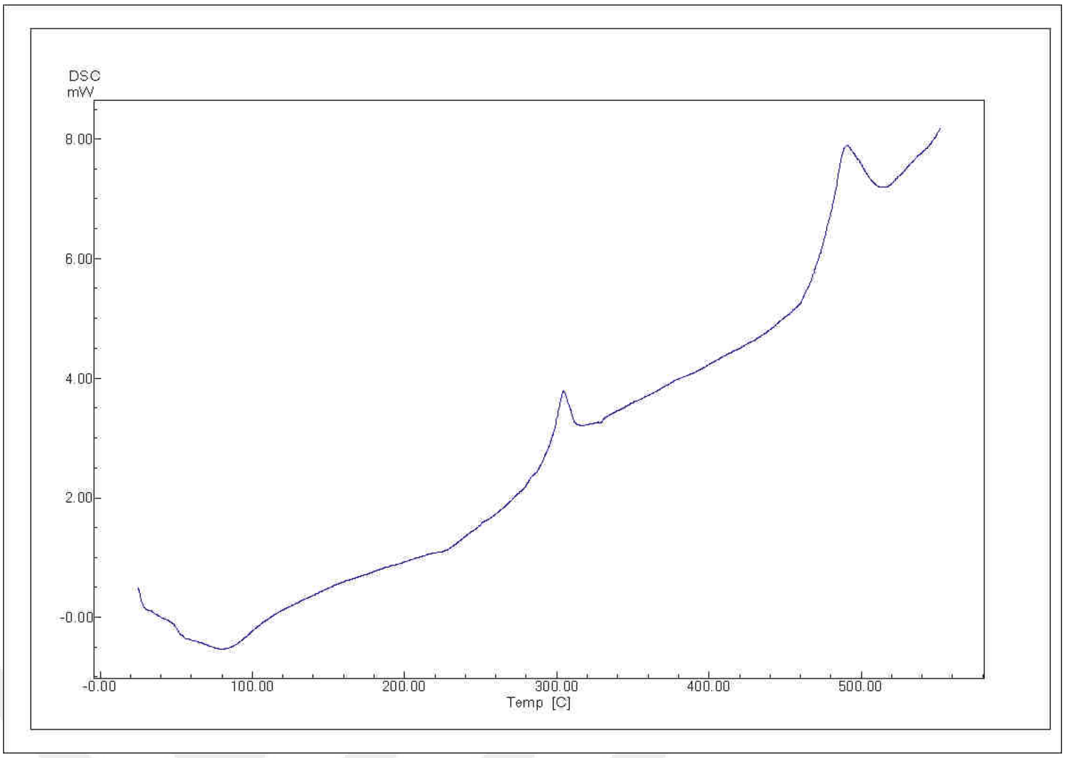

Figure 4.2 e) DSC thermogram of the ZnO NPs

4.3. Analysis of CS-ZnO NPs

The FTIR spectrum of the CS-ZnO NPs (Figure 4.3 a) was obtained using the ATR technique. At the peak between 3535-3020 cm^{-1} in the spectrum seen in the NH$_2$ and OH groups of Chitosan, the peaks are overlapped. The peaks observed specifically for chitosan are, CH$_3$ and CH$_2$ peaks between 2941-2814 cm^{-1} , C-H peak(weak) in the range 2000-1600 cm^{-1} , C-C peaks in the range 1583-1504 cm^{-1} and C-H peak in the range 1470-1340 cm^{-1}. C-O tensile peak is seen in the range of 1087-991 cm^{-1} (AbdElhady, 2012). The peak at between 590-540 cm^{-1} in the spectrum is specific for ZnO (Janaki et al., 2015).

The FTIR spectrum of the neat CS (Figure 4.3 b) was obtained using the ATR technique. The peak between 3640-3610 cm^{-1} assigned OH group and between 3535-3020 cm^{-1} in the spectrum of the NH$_2$ group. CH$_3$ and CH$_2$ peak is seen from to 2941-2814 cm^{-1}, C-H peak(weak) in the range 2000-1600 cm^{-1} , C-C peaks in the range of 1583-1504 cm^{-1} and C-H peak in the range of 1470-1340 cm^{-1} were determined. C-O tensile peak is seen in the range of 1087-991 cm^{-1}

(AbdElhady, 2012). Referring to Figure 4.3 a) and b), it is seen that ZnO NPs are coated with chitosan.

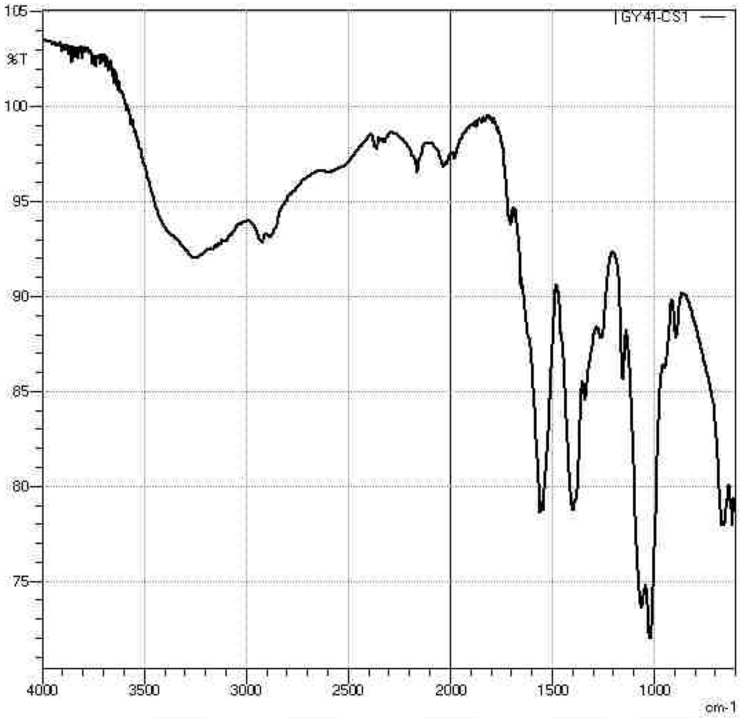

Figure 4.3 a) FTIR spectrum of the CS-ZnO NPs

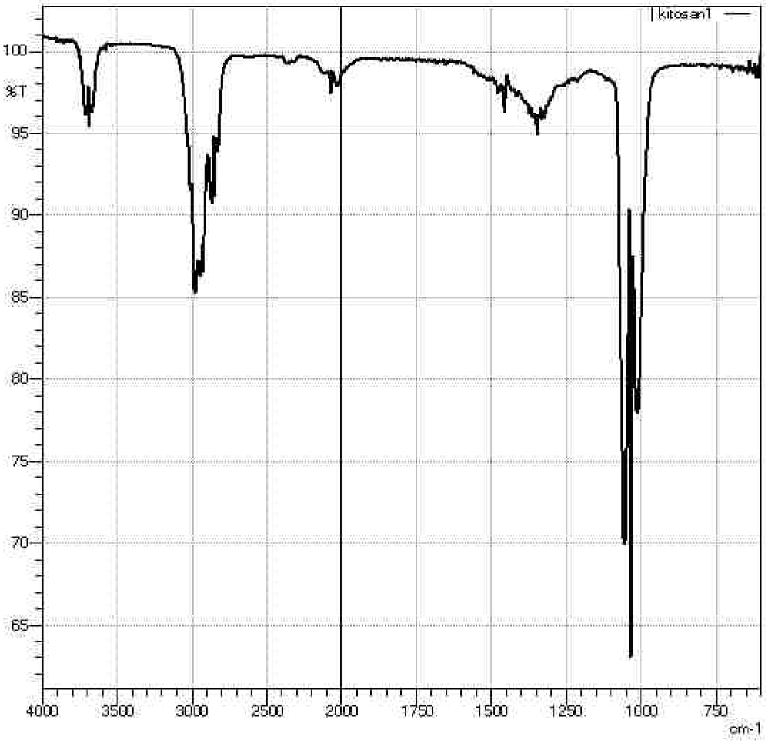

Figure 4.3 b) FTIR spectrum of the neat CS

The dimensions of the CS-coated ZnO NPs were measured by SEM analysis (Figure 4.3 c-e). The dimensions of the structure were measured between 75-116 nm.

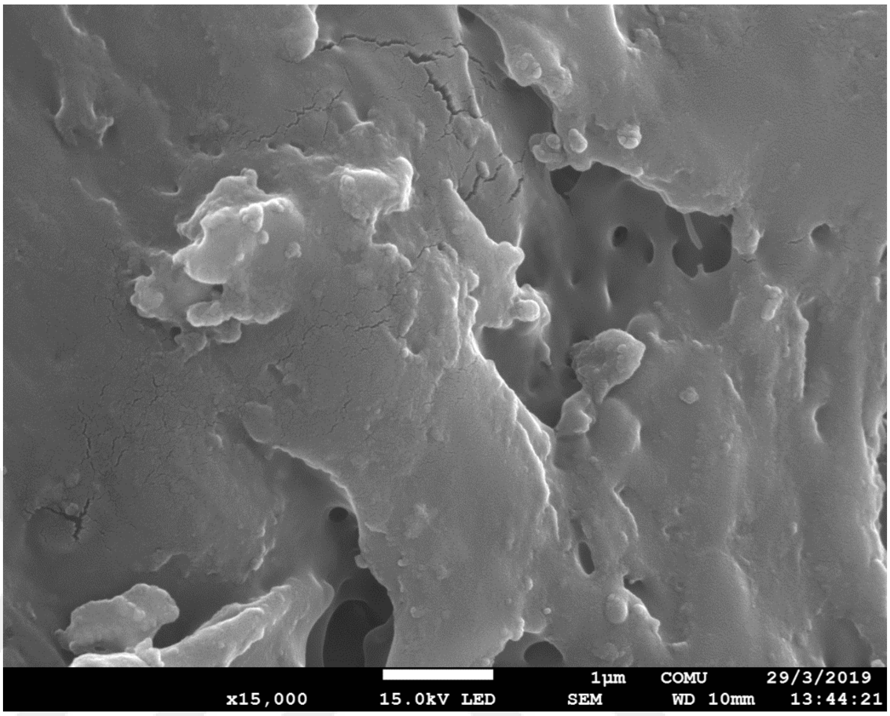

Figure 4.3 SEM image showing CS-ZnO NPs c) x15000 Focused CS-ZnO NPs

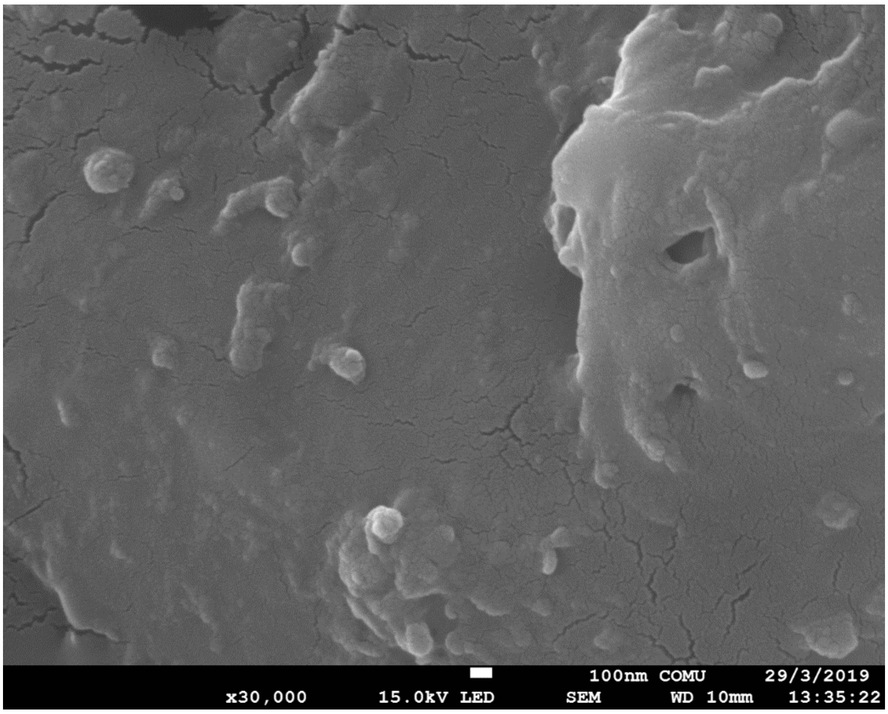

Figure 4.3 SEM image showing CS-ZnO NPs d) x30000 Focused CS-ZnO NPs

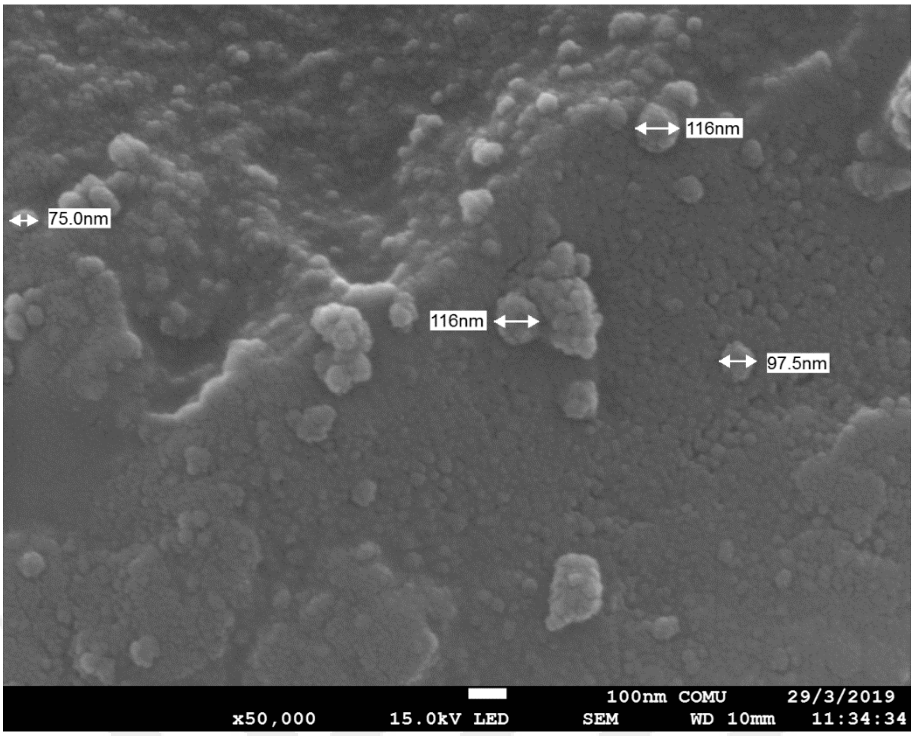

Figure 4.3 SEM image showing CS-ZnO NPs e) x50000 Focused CS-ZnO NPs

The dimensions of the ZnO NPs coated with the poly vinyl alcohol were determined by Mohan and B (2015) in SEM images at around 100 nm. In 2018, the study of Sawant and Bamane reported the synthesis of polyethylene glycol coated ZnO NPs. The SEM images of these structures show two morphological structures as rod and oval. In the literature, He et al. (2009), measured the dimensions of ZnO NPs coated with the polymer is at about 100 nm in SEM images. When SEM images of polymer-coated ZnO NPs in the literature are examined, it is seen that the SEM images of ZnO NPs synthesized with chitosan in this thesis were consistent with the literature.

TG/DTG measurements of CS-ZnO NPs were obtained using a heating rate of 10°C/min in a nitrogen atmosphere in the range of 30 to 1000°C temperatures. According to the thermograms in the Figure 4.3 f-g), there were three stages of degradation. The first mass loss was observed between 30-156°C at 13%, the second mass loss was between 156-336°C at 48%, and the third mass loss was between 336-461°C at 62%. The maximum decomposition temperatures (T_{max}) of the CS-ZnO NPs for first, second and third stages are observed at 111, 251 and 401°C , respectively. 38% of the structure comes from zinc. This is explained by the degradation of the polymer and the TG/DTG results confirm that the ZnO nanoparticles are coated with the CS. The thermograms are in good agreement with the literature (Soundhar and Jayakrishna, 2019).

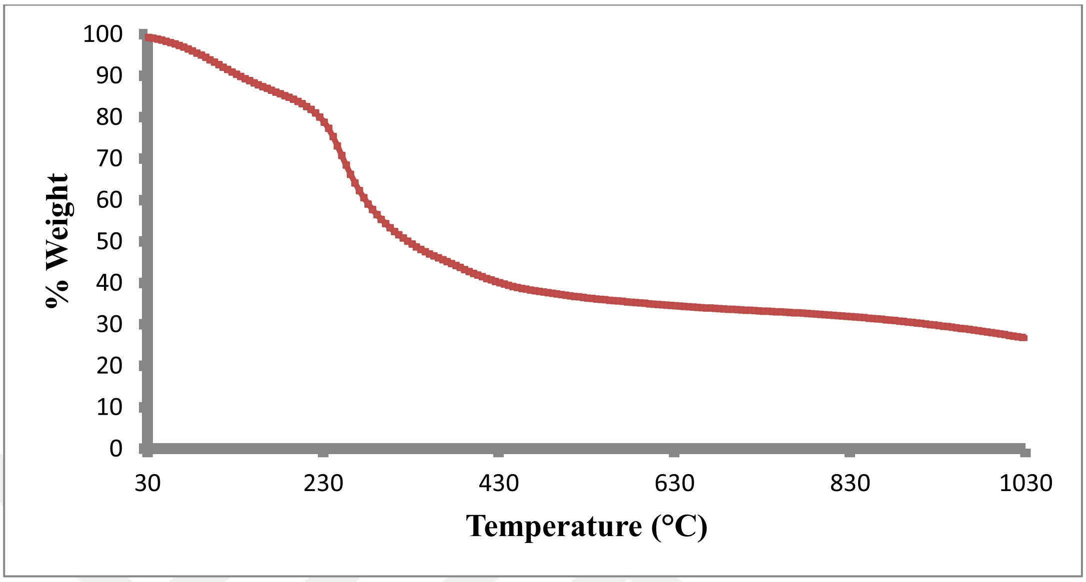

Figure 4.3 f) TG thermogram of the CS-ZnO NPs

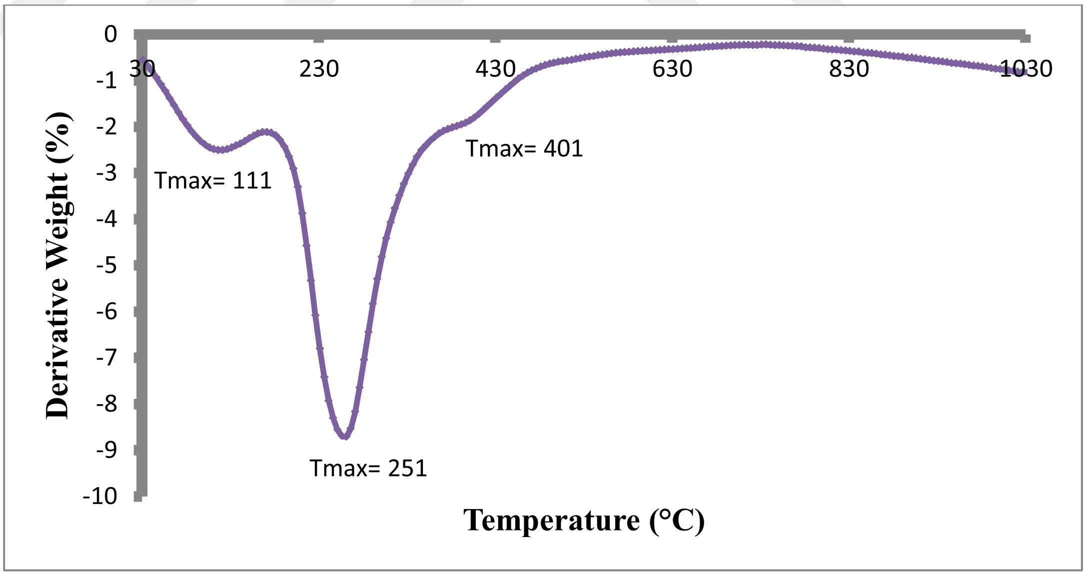

Figure 4.3 g) DTG thermogram of the CS-ZnO NPs

The synthesized CS-ZnO NPs were analyzed by DSC. All DSC measurements were made by heating 10°C/min under nitrogen at 50ml/min. The Figure 4.3 h) shows a 550°C exothermic peak. Other exothermic and endothermic peaks in the structure are structural defects resulting from the coating of ZnO nanoparticles with chitosan (Soundhar and Jayakrishna, 2019).

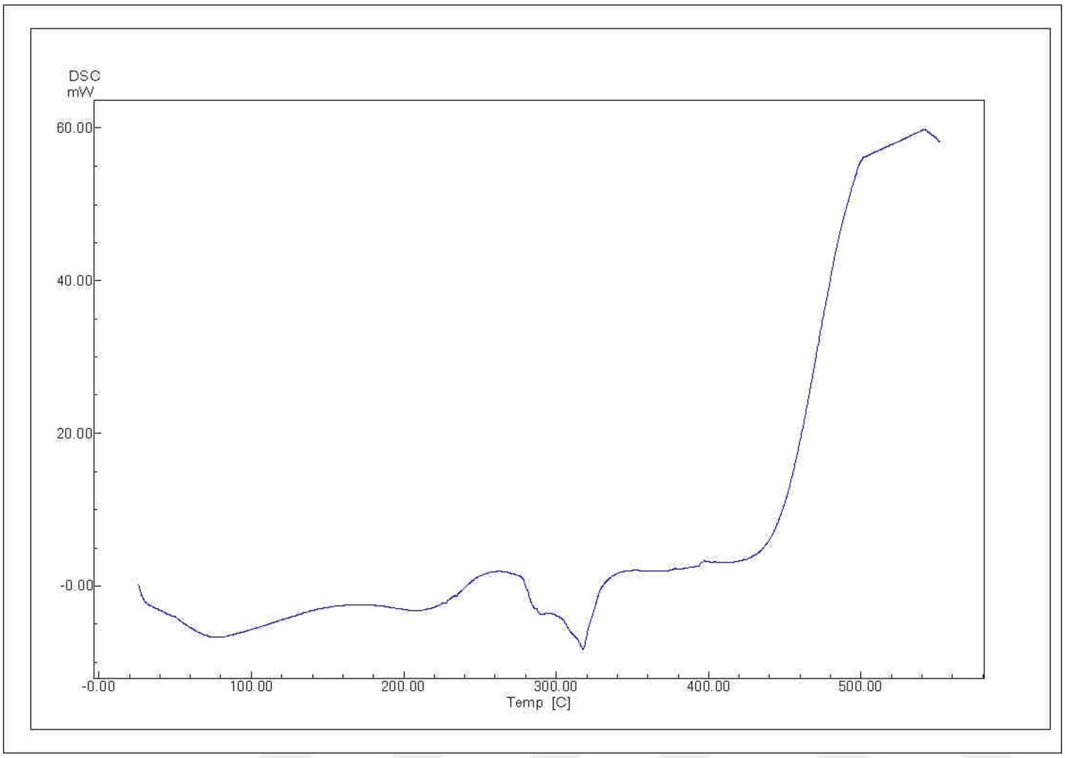

Figure 4.3 h) DSC thermogram of the CS-ZnO NPs

4.4. Analysis of Cafestol-CS-ZnO NPs

The FTIR spectrum of the Cafestol-CS-ZnO NPs (Figure 4.4 a) was obtained using the ATR technique. The spectrum shows the peak between 3402-2883 cm^{-1} in the spectrum seen in the NH_2 group. CH_3 and CH_2 peaks between 2347-2233 cm^{-1} , C=C peaks in the range 1566-1512 cm^{-1}, C-H peak in the range 1456-1359 cm^{-1} and C=O peak in the range of 1720-1716 cm^{-1}. C-O tensile peak is seen in the range of 1066-948 cm^{-1} and C-H bending peak is seen in the range of 1034-1032 cm^{-1} (Terrile et al., 2016).

Figure 4.4 b) also shows changes in structure when ligated to CS-ZnO NPs of Cafestol.

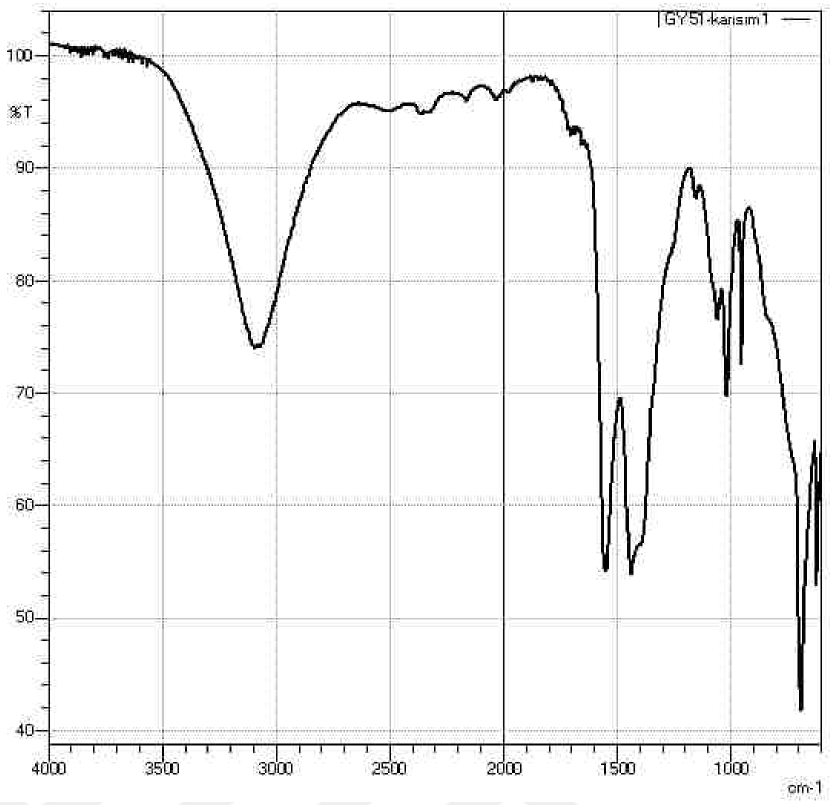

Figure 4.4 a) FTIR spectrum of the Cafestol-CS-ZnO NPs

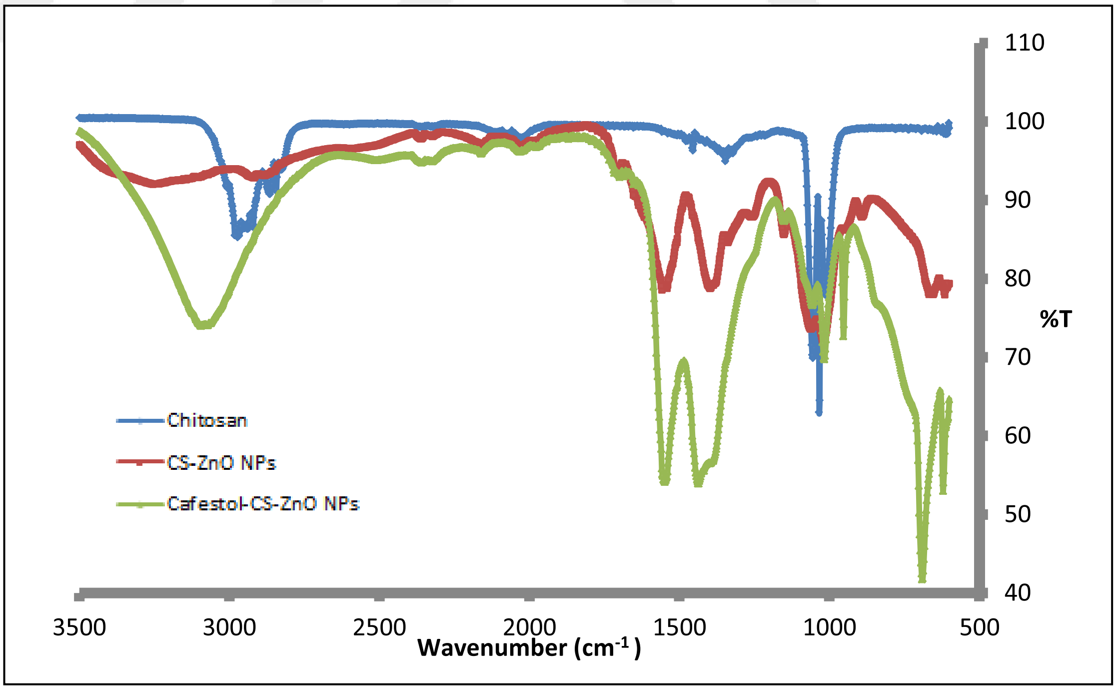

Figure 4.4 b) FTIR spectra of the Cafestol-CS-ZnO NPs, CS-ZnO NPs and Chitosan

Cafestol-CS-ZnO NP structure, which was formed after cafestol binding to CS-ZnO NPs, was analyzed by SEM images (Figure 4.4 c-e).

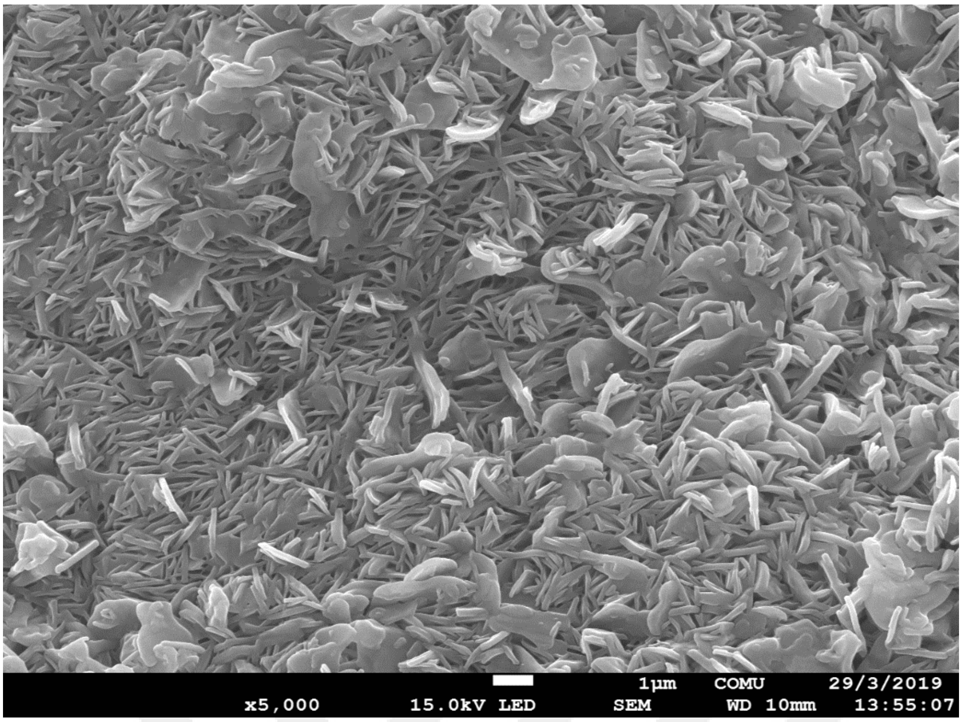

Figure 4.4 SEM image showing Cafestol-CS-ZnO NPs c) x5000 Focused Cafestol-CS-ZnO NPs

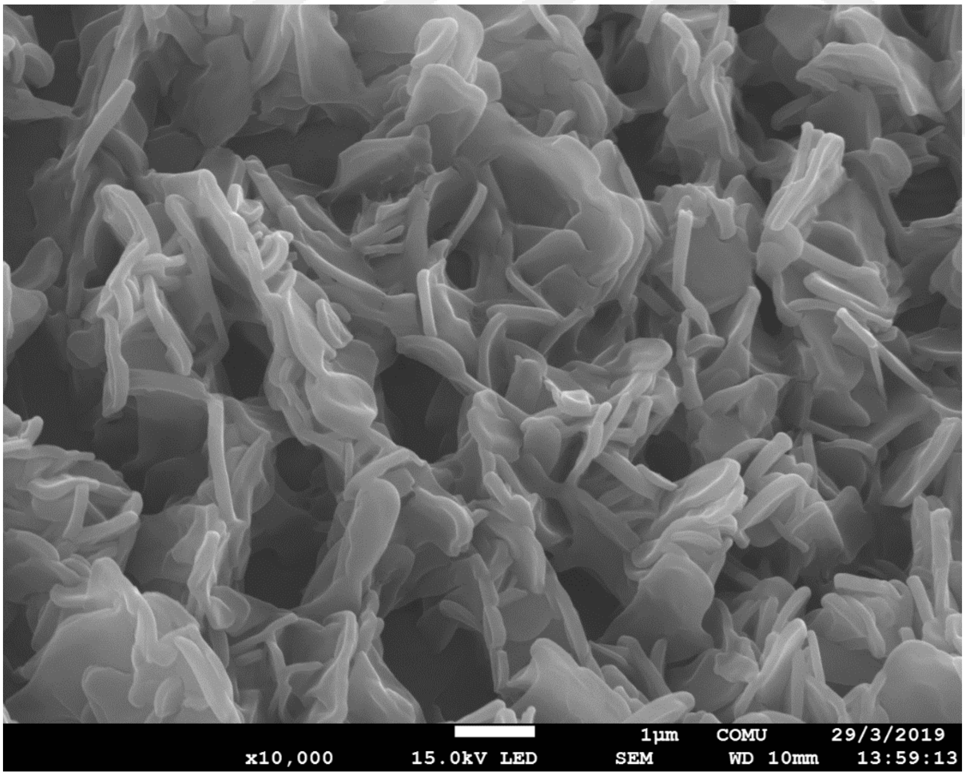

Figure 4.4 SEM image showing Cafestol-CS-ZnO NPs d) x10000 Focused Cafestol-CS-ZnO NPs

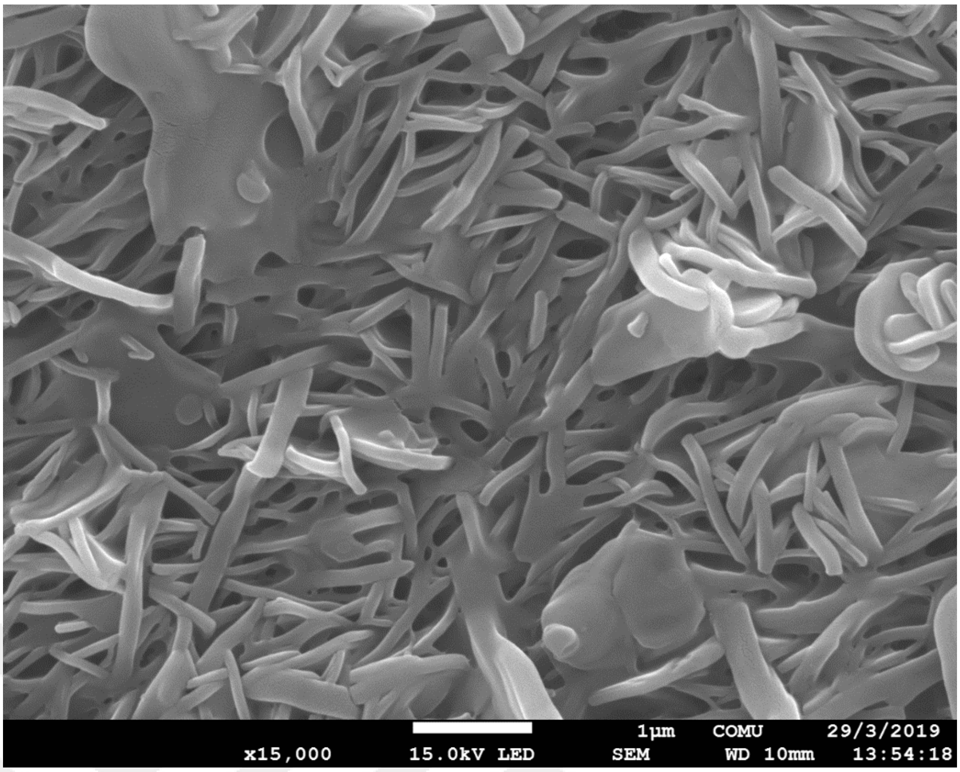

Figure 4.4 SEM image showing Cafestol-CS-ZnO NPs e) x15000 Focused Cafestol-CS-ZnO NPs

The SEM images show that the structure is formed as rods. The Cafestol-CS-ZnO NPs show a branched morphology and are connected to each other as long structures.

TG/DTG measurements of Cafestol-CS-ZnO NPs were obtained using a heating rate of 10^{o}C/min in a nitrogen atmosphere in the range of 30 to 1000^{o}C temperatures. According to the Figure 4.4 f-g) shown, there are three degradation stages for Cafestol-CS-ZnO. The first mass loss was observed between 30-161^{o}C at 11%, the second mass loss was between 161-316^{o}C at 48%, and the third mass loss was between 316-431^{o}C at 61%. T_{max} of the Cafestol-CS-ZnO NPs for first, second and third stages are observed at 106, 241 and 361^{o}C , respectively. The TG of Cafestol-CS-ZnO NPs molecule gives almost 25% residues even at 1000 ^{o}C. When the thermograms in Figure 4.2 d) and Figure 4.3 g) are compared, the differences in the thermograms indicate that the cafestol is connected to the structure.

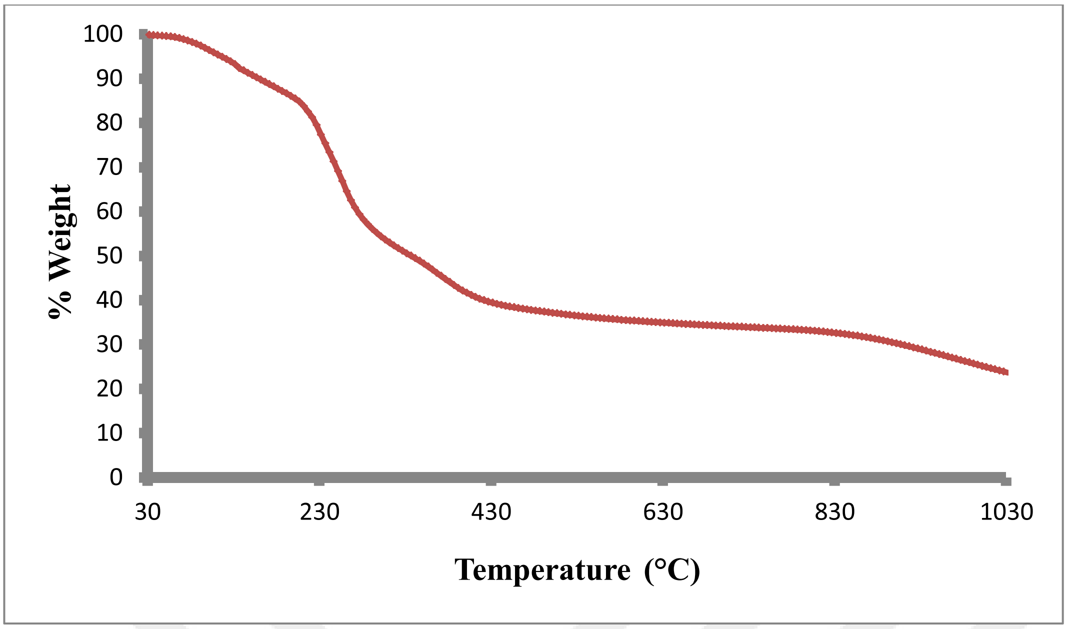

Figure 4.4 f) TG thermogram of the Cafestol-CS-ZnO NPs

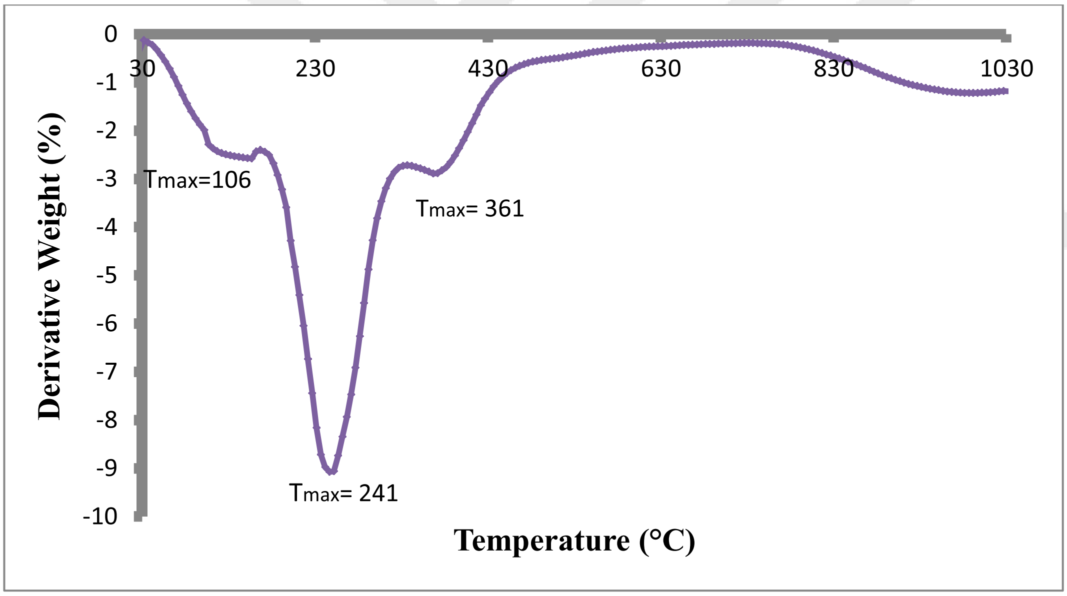

Figure 4.4 g) DTG thermogram of the Cafestol-CS-ZnO NPs

The synthesized Cafestol-CS-ZnO NPs were analyzed by DSC. All DSC measurements were made by heating 10^{o}C/min under nitrogen at 50ml/min. The DSC thermogram of Cafestol-CS-ZnO nanoparticles (Fig. 4.4 h), CS-ZnO NPs and ZnO NPs are seen to differ according to their DSC thermograms.

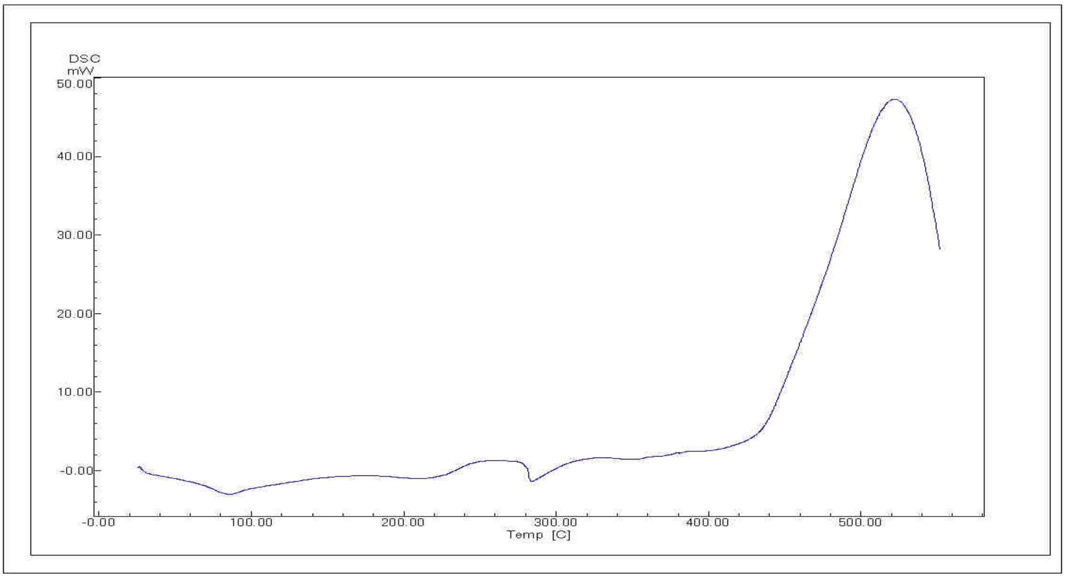

Figure 4.4 h) DSC thermogram of the Cafestol-CS-ZnO NPs

A calibration graph (Figure 4.4 i) was drawn using UV spectrophotometry at 244 nm with the cafestol solution obtained with ethanol. Cafestol-CS-ZnO NPs were found to have a 15% cafestol binding yield.

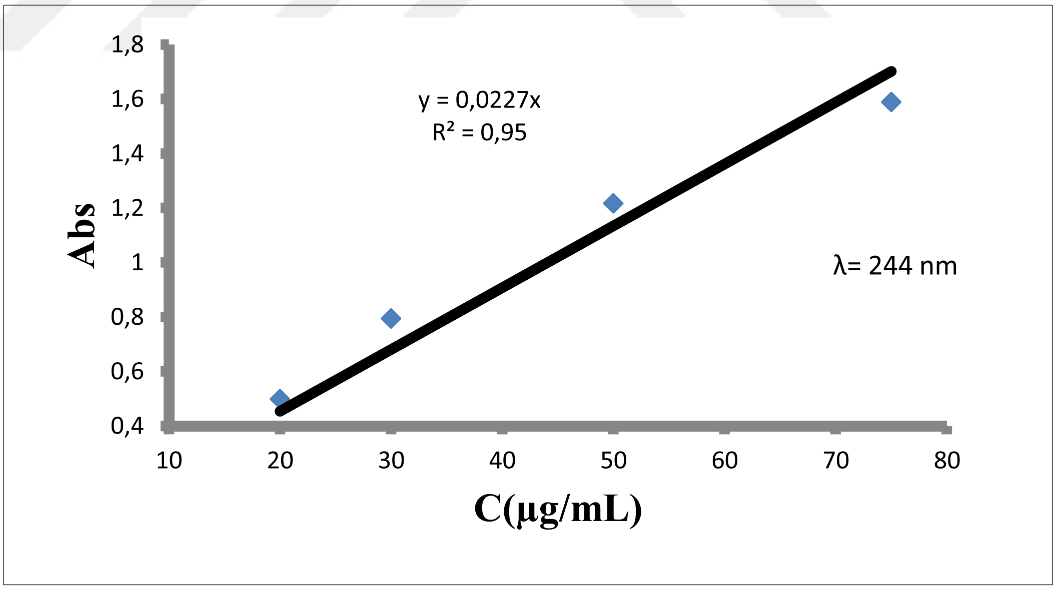

Figure 4.4 i) The calibration graph of the cafestol by using UV spectrophotometer

5. CONCLUSION

In this thesis, the synthesis of ZnO NPs which have antimicrobial properties was performed and chitosan was coated to the synthesized ZnO NPs and cafestol was ligated to the CS-ZnO NP structures. Zeta Sizer, SEM, FTIR, DSC and TG devices were used for analysis of ZnO NPs, CS-ZnO NPs and Cafestol-CS-ZnO NPs.

Zinc oxide nanoparticles were produced by chemical precipitation method. Optimization studies were performed to obtain the desired size of ZnO NP. In optimization studies, it was seen that Zn salt, salt concentration, base type, mixing speed, calcination temperature and reaction time are important for the size of ZnO NPs. For the synthesis of the desired size ZnO NPs, 0.2 M $Zn(SO_4)$ salt was precipitated with NaOH and calcined at 400^oC.

The spectra of the structures synthesized as a result of FTIR analysis are examined, it is seen that they are in consistent with the reported spectra in the literature.

As a result of the size analysis with SEM images ZnO NPs were found between 45 and 60 nm dimensions and have spherical and hexagonal morphology. The size of CS-ZnO NPs found to be in the range of 75-116 nm. In the SEM images, the structure of Cafestol-CS-ZnO NP was rod-shaped and showed morphological structure changes.

As a result of the thermal analyzes DSC / TG / DTG, structural differences were observed and the synthesis of Cafestol-CS-ZnO NPs was realized successfully. In addition, according to UV calibration graph shows that the ratio of cafestol ligated to CS-ZnO NPs is 15%.

Furthermore, in order to investigate the efficacy of synthesized Cafestol-CS-ZnO NPs in wound treatment, Cafestol-CS-ZnO NPs are planned to be used in in-vitro studies.

REFERENCES

AbdElhady, M.M., 2012, Preparation and characterization of chitosan/zinc oxide nanoparticles for imparting antimicrobial and UV protection to cotton fabric, International Journal of Carbohydrate Chemistry, 2012, 6p.

Allahverdiyev, M.A., Abamar, S.E., Bagırova, M. and Rafailovich, M., 2011, Antimicrobial effects of TiO_2 and Ag_2O nanoparticles against drug-resistant bacteria and leishmania parasites, Future Microbiology, 6(8).

Bahl, R., Bhandari, N., Hambidge, K.M. and Bhan, M.K., 1998, Plasma zinc as a predictor of diarrheal and respiratory morbidity in children in an urban slum setting, The American Journal of Clinical Nutrition, 68, 414-417p.

Berg, J.M. and Shi, Y., 1996, The galvanization of biology: a growing appreciation for the roles of zinc, Science, 271, 1081-1085p.

Besinis, A., Peralta, D.T. and Handy, D.R., 2012, The antibacterial effects of silver, titanium dioxide and silica dioxide nanoparticles compared to the dental disinfectant chlorhexidine an streptococcus mutans using a suite of bioassays, Nanotoxicology, 8, 1-16p.

Bhutta, Z.A., Black, R.E., Brown, K.H., Gardner, J.M., Gore, S., Hidayat, A., Khatun, F., Mortorell, R., Ninh, N.X., Penny, M.E., Rosado, J.L., Roy, S.K., Ruel, M., Sazawall, S. and Shankar, A., 1999, Prevention of diarrhea and pneumonia by zinc supplementation in children in developing countries: pooled analysis of randomized controlled trials, Journal of Pediatrics, 135, 689-697p.

Bilensoy, E., Erdoğar, N. ve Munan, N.A., 2015, Kasa invaze olmayan mesane kanserinin tedavisinde nanopartiküllerin rolü, Üroonkoloji Bülteni, 14, 61-66s.

Buzea, C., Pacheco, I.I. and Robbie, K., 2007, Nanomaterials and nanoparticles: sources and toxicity, Biointerphases, 2(4), 17-71p.

Caltech, 1960, There's plenty of room at the bottom, Caltech Engineering and Science, 23(5), 22-36p.

REFERENCES (Continue)

Chaudhry, Q., Scatter, M., Blackburn, A., Castle, L., Aitken, R. and Watkins, R., 2008, Applications and implications of nanotechnologies for the food sector, Food Additives and Contaminants, 25(3), 241-258p.

Chesters, J.K., 1982, Metabolism and biochemistry of zinc, 221-234p., Clinical Biochemistry of Nutritional Aspects of Trace Element, A. Prasad (Ed.).

Cho, Y.W., Chung, S.H., Yoo, G. and Ko, S.W., 1999, Water soluble chitin as a wound healing acceleration, Biomaterials, 20, 2139-2145p.

Demir, A. ve Seventekin, N., 2009, Kitin, kitosan ve genel kullanım alanları, Tekstil Teknolojileri Elektronik Dergisi, 3(2), 92-103p.

Dizaj, M.S., Lotfipour, F., Jalali, B.M., Zarintan, H.M. and Adibkia, K., 2014, Antimicrobial activity of the metals and metal oxide nanoparticles, Material Science and Engineering C, 44, 278-284p.

Doğan, G., Şenol, F., Tayyar, E. ve Yaman, N., 2005, Karbon nanotüpler, Tekstil ve Konfeksiyon, 3, 135-138s.

Drude, N., Tienken, L. and Mottaghy, M.F., 2017, Theranostic and nanotheranostic probes in nuclear medicine, Methods, 130, 14-22p.

Dwivedi, S., Wahab, R., Khan, F., Mishra, K.Y., Musarrat, J. and Al-Khedhairy, A.A., 2014, Reactive oxygen species mediated bacterial biofilm inhibition via zinc oxide nanoparticles and their statistical determination, Plos One, 9(11).

Edelstein, A.S. and Commorata, R.C., 2001, Nanomaterials: synthesis, properties and applications, Institute of Physics Publishing.

Erkoç, Ş., 2014, Nanobilim ve nanoteknoloji, http://maycalistaylari.comu.edu.tr/maycalistaylari/phocadownload/userupload/lise4/davetlikonusmaci (Erişim tarihi: 5 Mart 2019).

Fierke, C., 2000, Function and mechanism of zinc, Journal of Nutrition, 130, 1437-1446p.

REFERENCES (Continue)

Ghishan, F.K., 1984, Transport of electrolytes, water and glucose in zinc deficiency, Journal of Pediatric Gastroenterology and Nutrition, 3, 608-612p.

Ghosh, T., 2005, The base of molecular nanotechnology and its implication in textiles, 39-43p.

Gnanasangeetha, D. and SaralaThambavani, D., 2013, One pot synthesis of zinc oxide nanoparticles via chemical and green method, Research Journal of Material Sciences, 1(7), 1-8p.

Goldstain, A., 1997, Handbook of nanophase materials, Marcel Dekker Inc., New York.

Gu, H., Chao, J., Xiao, J.J. and Seeman, N.C., 2009, Dynamic patterning programmed by DNA tiles captured on a DNA origami substrate, Nature Nanotechnology, 4(4), 245-248p.

Gu, H., Chao, J., Xiao, J.J. and Seeman, 2010, A proximity-based programmable DNA nanoscale assembly line, Nature, 465, 202-205p.

Gürmen, S. ve Ebin, B., 2008, Nanopartiküller ve üretim yöntemleri-1, Metalurji Dergisi, 31-38s.

Hambidge, M., 2000, Zinc and health: current status and future directions, American Society for Nutritional Sciences, 22, 1344-1349p.

He, J., Shao, W., Zhang, L., Deng, C. and Li, C., 2009, Crystallization behavior and UV-protection property of PET-ZnO nanocomposites prepared by In Situ polymerization, Journal of Applied Polymeric Science, 114, 1303-1311p.

Huber, W.W., McDaniel, L.P., Kaderlik, K.R., Teitel, C.H., Long, N.P. and Kadlubar, F.F., 1997, Chemoprotection against the formation of colon DNA adducts from the food-borne carcinogen 2-amino-1-methyl-6-phenylimidazol[4,5-b]pyridine (PhIP) in the rat, Mutation Research, 376, 115-122p.

REFERENCES (Continue)

IARC, 1991, IARC Monographs on the evaluation of the carcinogenic risks to humans, IARC(Ed.), World Health Organization, 41-206p., Lyon.

Ilves, M., Palomaki, J., Vippola, M., Lehto, M., Savolainen, K., Savinko, T. and Alenius, H., 2014, Topically applied ZnO nanoparticles suppress allergen induced skin inflammation but induce vigorous IgE production in the atopic dermatitis mouse model, Particle and Fibre Toxicology, 11(38).

Janaki, C.A., Sailatha, E. and Gunasekaran, S., 2015, Synthesis, characteristics and antimicrobial activity of ZnO nanoparticles, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 144, 17-22p.

Jiang, H., Wang, H. and Wang, X., 2011, Facile and mild preparation of fluorescent ZnO nanosheets and their bioimaging applications, Applied Surface Science, 257(15), 6991-6995p.

Jong, H.D., Hwang, D.W., Kim, D.P., Kim, H.C., Lee, B.Y. and Jeong, J.B., 2004, Preparation of cobalt nanoparticles by hydrogen reduction of cobalt chloride in the gas phase, Materials Research Bulletin, 39, 63-70p.

Kerman, K., Saito, M., Tamiya, E., Yamamura, S. and Takamura, Y., 2008, Nanomaterial-based electrochemical biosensors for medical applications, TrAC Trends in Analytical Chemistry, 27(7), 585-592p.

Kim, K.H., Aravindan, V., Mhamane, D., Yoon, B.S., Park, H.S., Samani, M., Han, T.J., Park, S.H., Roh, C.K. and Kim, B.K., 2018, Bulk metal-derived metal oxide nanoparticles on oxidized carbon surface, Journal of Alloys and Compounds, 752, 198-205p.

Koutu, V., Ojha, P., Shastri, L. and Malik, M.M., 2018, Study of the effect of temperature gradient on the thermal and electrical properties of ZnO nanoparticles, AIP Conference Proceedings, 1953.

Kumar, S.P.T., Lakshmanan, V.K., Anilkumar, T.V., Ramya, C., Reshmi, P., Unnikrishnan, A.G., Nair, V.S. and Jayakumar, R., 2012, Flexible and microporous chitosan hydrogel/nano ZnO composite bandages for wound dressing: in vitro and in vivo evaluation, ACS Applied Materials & Interfaces, 4, 2618-2629p.

REFERENCES (Continue)

Kumar, S.S., Venkateswarlu, P., Rao, R.V. and Rao, N.G., 2013, Synthesis, characterization and optical properties of zinc oxide nanoparticles, International Nano Letters, 3(30), 1-6p.

Lee, D.W., Power, K. and Boney, R., 2004, Physicochemical properties and blood compatibility of acylated chitosan nanoparticles, Carbohydrate Polymers, 58, 371-377p.

Lee, K.J. and Jeong, H.G., 2007, Protective effects of kahweol and cafestol against hydrogen peroxide-induced oxidative stress and DNA damage, Toxicology Letters, 173(2), 80-87p.

Lipovsky, A., Nitzan, Y., Gedanken, A. and Lubart, R., 2011, Antifungal activity of ZnO nanoparticles-the role of ROS mediated cell injury, Nanotechnology, 22(10), 5p.

Liu, Y. and Chen, C., 2016, Role of nanotechnology in HIV/AIDS vaccine development, Advanced Drug Delivery, 103, 76-89p.

Liveri, V.T., 2006, Controlled synthesis of nanoparticles in microheterogeneous systems, Springer Science + Business Media Inc., New York.

Malarkodi, C., Rajeshkumar, S., Paulkumar, K., Vanaja, M., Gnanajobitha, G. and Annadural, G., 2014, Biosynthesis and antimicrobial activity of semiconductor nanoparticles against oral pathogens, Bioinorganic Chemistry and Applications, 2014, 10p.

Mohan, C. and B, R., 2016, Preparation of zinc oxide nanoparticles and its characterization using scanning electron microscopy (SEM) and X-Ray diffraction (XRD), Procedia Technology, 24, 761-766p.

Nazarizadeh, A. and Asri-Rezaie, S., 2015, Comparative study of antidiabetic activity and antioxidative stress induced by zinc oxide nanoparticles and zinc sulfate in diabetics rats, AAA PharmSciTech, 17(4), 834-843p.

Neethirajan, S. and Jayas, D.S., 2011, Nanotechnology for the food and bioprocessing industries, Food Bioprocess Technology, 4, 39-47p.

REFERENCES (Continue)

Özbay, E. and Gülce, H., 2014, Çinko oksit nanopartikülleri sentezi ve karakterizasyonu, Selçuk Üniversitesi Mühendislik Bilim ve Teknoloji Dergisi, 2(4).

Peng, Q. and Qin, Y., 2011, Intech Open, 10.

Qu, F. and Morais, P.C., 2001, The pH dependence of the surface charge density in oxide-based semiconductor nanoparticles immersed in aqueous solution, IEEE Transection on Magnetics, 37(4), 2654-2656p.

Rasmussen, W.J., Martinez, E., Louka, P. and Wingett, G.D., 2010, Zinc oxide nanoparticles for selective destruction of tumor cells and potential for drug delivery applications, Expert Opinion on Drug Delivery, 7(9), 1063-1077p.

Roth, P., 2007, Particle synthesis in flames, Proceedings of Combustion Institute, 31, 1773-1788p.

Sawant, J.V. and Bamane, R.S., 2018, PEG-beta-cyclodextrin functionalized zinc oxide nanoparticles show cell imaging with high drug payload and sustained pH responsive delivery of curcumin in to MCF-7 cells, Journal of Drug Delivery Science and Technology, 43, 397-408p.

Seil, J.T. and Webster, T.J., 2012, Antimicrobial applications of nanotechnology methods and literature, International Journal of Nanomedicine, 7, 2767-2781p.

Shahidi, F., **Arachchi, J.K.V. and Jeon, Y.J.,** 1999, Food applications of chitin and chitosans, Trends in Food Science & Technology, 10, 37-51p.

Sheini, J.F., 2012, Chemical solution deposition of ZnO nanostructure films: morphology and substrate angle dependency, Ceramics International, 38(5), 3649-3657p.

Shirai, Y., Osgood, J.A., Zhao, Y., Kelly, F.K. and Tour, M.J., 2005, Directional control in thermally driven single-molecules nanocars, NanoLetters, 5(11), 2330-2334p.

REFERENCES (Continue)

Shoundhar, A. and Jayakrishna, K., 2019, Investigations on mechanical and morphological characterization of chitosan reinforced polymer nanocomposites, Materails Research Express, 6(7).

Singh, K.K., Desovki, M.M., Franklin, R.B. and Costello, L.C., 2006, Mitochondrial acconitase and citrate metabolism in malignant and nonmalignant human prostate tissues, Molecular Cancer, 5, 14p.

Song, W., Musetti, N.S. and Huang, L., 2017, Nanomaterials for cancer immunotherapy, Biomaterials, 148, 16-30p.

Srivastava, V., Gusain, D. and Sharma, C.Y., 2013, Synthesis, characterization and application of zinc oxide nanoparticles (n-ZnO), Ceramics International, 39, 9803-9808p.

Suh, H.J., Jong, H.D., Chang, H., Kim, W.B. and Kim, H.C., 2006, Size-controlled synthesis of Fe-Ni alloy nanoparticles by hydrogen reduction of metal chlorides, Powder Technology, 161, 196-201p.

Suri, S.S., Fenniri, H. and Singh, B., 2007, Nanotechnology-based drug delivery systems, Journal of Occupational Medicine and Toxicology, 2(16).

Süfer, Ö. ve Karakaya, S., 2011, Gıda endüstrisi ve nanoteknoloji: durum tespiti ve gelecek, Akademik Gıda, 9(6), 81-88s.

Terrile, E.A., Marcheafave, G.G., Oliveira, S.G., Rakocevic, M., Bruns, E.R. and Scarminin, S.I., 2016, Chemometric analysis of UV characteristic profile and infrared fingerprint variations of coffea Arabica green beans under different space management treatments, Journal of the Brazilian Chemical Society, 27(7), 1254-1263p.

Tsai, S.C., Song, Y.L., Tsai, C.S., Yang, C.C., Chiu, W.Y. and Lin, H.M., 2004, Ultrasonic spray pyrolysis for nanoparticles synthesis, Journal of Material Science, 39, 3647-3657p.

Tseng, Y.K., Chuang, M.H., Chen, Y.C. and Wu, C.H., 2012, Synthesis of 1D, 2D and 3D ZnO polycrystalline nanostructures using the Sol-Gel method, Journal of Nanotechnology, 2012, 8p.

REFERENCES (Continue)

Tunca, Ü.E., 2015, Nanoteknolojinin temeli nanopartiküller ve nanopartiküllerin fitoremediasyonu, Ordu Üniversitesi Bilim ve Teknoloji Dergisi, 5(2), 23-24s.

Tuncer, S., 2014, Çoklu ilaca dirençli kanser hücre hattına nanopartiküllerle ilaç aktarımı, Yüksek Lisans Tezi, Hacettepe Üniversitesi, 101s.

Turgut, O., Keskin, H.L. ve Avşar, A.F., 2011, Nanoteknoloji nedir?, Türkiye Tıp Dergisi, 5(1), 45-49p.

Ubani, A.C. and Ibrahim, A.M., 2019, Complementary processing methods for ZnO nanoparticles, Materials Today: Proceeding, 7, 646-654p.

Villaverde, A. and Rodriguez-Carmona, E., 2010, Nanostructured bacterial materials for innovative medicines, Trends in Microbiology, 18(9), 423-430p.

Walravens, P.A., VanDoorninck, W.J. and Hambidge, K.M., 1978, Metals and mental function, Journal of Pediatrics, 93, 535p.

Wang, Z.H., Choi, C.J., Kim, B.K., Kim, J.C. and Zhang, Z.D., 2003, Characterization of Fe-Co alloyed nanoparticles synthesized by chemical vapor condensation, Materials Letters, 57, 3560-3564p.

Williams, R.J.P., 1989, An introduction to the biochemistry of zinc, 15-31p., Zinc in Human Biology, F.C., Mills (Ed.).

World Health Organization, 2018, Cancer Fact Sheet, http://www.who.int/en/news-room/fact-sheets/detail/cancer (Erişim tarihi: 19 Kasım 2018).

Xu, L., Guo, Y., Liao, Q., Zhang, J. and Xu, D., 2005, Morphological control of ZnO nanostructures by electrodeposition, Journal of Physical Chemistry B, 109, 13519-13522p.

Yıldırım, Y., 2003, Study of the relations between zinc and β-glucuronidase levels in some biological tissues using a new nuclear measurement technique for β-glucuronidase, MSc Thesis, Ege Univesity, 94p.

REFERENCES (Continue)

Zikalala, N., Matshetshe, K., Parani, S. and Oluwafemi, S.O., 2018, Biosynthesis protocols for colloidal metal oxide nanoparticles, Nano-Structures & Nano-Objects, 16, 288-299p.

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