

Dilber Akcan

M.Sc. Thesis

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PLANT-MEDIATED SUSTAINABLE NANOMATERIALS FOR BIOMEDICAL AND OPTICAL APPLICATIONS

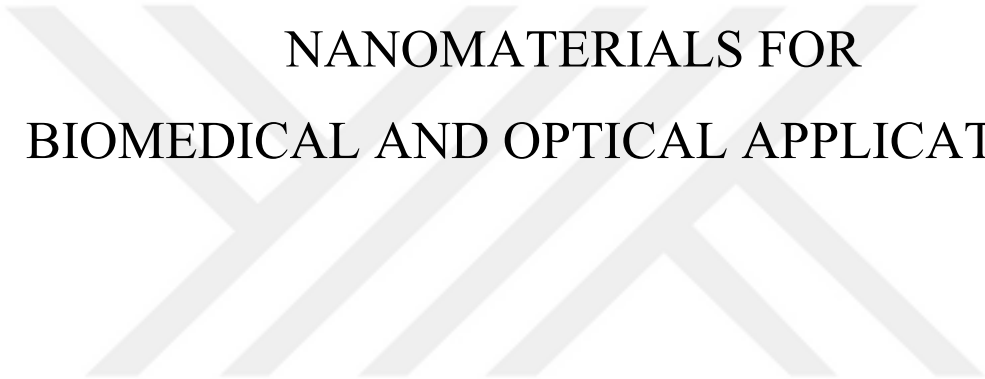
M.Sc. THESIS

SUBMITTED TO THE DEPARTMENT OF BIOENGINEERING
AND THE GRADUATE SCHOOL OF ENGINEERING AND SCIENCE
OF ABDULLAH GUL UNIVERSITY
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
MASTER

By

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Signature:



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Prepared By

Dilber AKCAN

Signature

Advisor

Asst. Prof. Zeliha SORAN ERDEM

Signature

Head of the Bioengineering Program

Asst. Prof. Emel Başak GENCER AKÇOK

Signature

ACCEPTANCE AND APPROVAL

M.Sc. thesis titled Plant-mediated Sustainable Nanomaterials for Biomedical and Optical Applications and prepared by Dilber AKCAN has been accepted by the jury in the Bioengineering Graduate Program at Abdullah Gül University, Graduate School of Engineering & Science.

09/ 01 / 2025

JURY:

Advisor: Asst. Prof. Zeliha SORAN ERDEM

Member: Asst. Prof. Talha ERDEM

Member: Prof Dr. İsmail ÖÇSOY

APPROVAL:

The acceptance of this M.Sc. thesis has been approved by the decision of the Abdullah Gül University, Graduate School of Engineering & Science, Executive Board dated / / and numbered

..... / /

(Date)

Graduate School Dean
Prof. İrfan ALAN

ABSTRACT

PLANT-MEDIATED SUSTAINABLE NANOMATERIALS FOR BIOMEDICAL AND OPTICAL APPLICATIONS

Dilber AKCAN
MSc. in Bioengineering
Advisor: Asst. Prof. Zeliha SORAN ERDEM
January 2025

Plant-mediated nanomaterials have gained significant attention in biomedical and optical studies because of their biological and optical properties. For that reason, we focused on two different plant extracts (*Hypericum perforatum* and *Peganum harmala*) in biomedical and optical applications. In the first part of this thesis, we synthesized zinc oxide nanoparticles (ZnO NPs) using *Hypericum perforatum* via an environmentally friendly green synthesis method. Nanoparticles were characterized using UV-Vis spectroscopy, X-ray diffraction (XRD), scanning electron microscopy (SEM), and energy dispersive X-ray (EDX) analyses. The anticancer effect of these nanoparticles was investigated against the human liver cancer cell (Hep-G2) with cell culture studies. Finally, the antibacterial activity of the ZnO NPs was studied. Cell viability studies demonstrated a NP dose-dependent inhibition of cell viability along with significant cytotoxic effects at higher concentrations. With this study, we showed that these ZnO NPs have extremely high potential as therapeutics for liver cancer treatment. In the second part of this thesis, we designed a paper-based color converter using *Peganum harmala* extract for solid-state lighting. Due to the high quantum yield of the plant extract in the solid state, fluorescent biomolecules from the plant extract were wrapped into crystal-based (sucrose and KCl crystals) and cellulose fiber-based (cotton pads and drying papers) matrices. Optical characterizations demonstrated high quantum efficiency in the fiber paper group. As a proof-of-concept demonstration, *P. harmala* extract embedded fiber paper was used as a color converter on an LED, and the device revealed a blue emission with a luminous efficiency of $21.9 \text{ lm W}_{\text{elect}}^{-1}$. The results showed that these environmentally friendly plant-based materials can replace the currently used color converters as their cost-effective and sustainable alternatives.

Keywords: *Plant-mediated nanomaterials; Hypericum Perforatum; Peganum harmala; zinc oxide nanoparticles; color converter*

ÖZET

BİYOMEDİKAL VE OPTİK UYGULAMALAR İÇİN BİTKİ ARACILI SÜRDÜRÜLEBİLİR NANOMALZEMELER

Dilber Akcan

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Bitki aracılı nanomalzemeler biyomedikal ve optik çalışmalarda önemli bir ilgi görmüştür. Bu nedenle, biyomedikal ve optik uygulamalarda iki farklı bitki özütünü (*Hypericum Perforatum* ve *Peganum harmala*) araştırdık. Bu tezin ilk bölümünde, çevre dostu yeşil sentez yöntemi ile *Hypericum Perforatum* kullanarak çinko oksit nanopartikülleri (ZnO NP'leri) sentezledik. Nanopartiküller UV-Vis spektroskopisi, X-ışını kırınımı (XRD), taramalı elektron mikroskobu (SEM) kullanılarak karakterize edildi. Bu nanopartiküllerin antikanser etkisi, hücre kültürü çalışmalarıyla insan karaciğer kanseri hücrelerinde (Hep-G2) test edildi. Son olarak, bu ZnO NP'lerin anti bakteriyel aktivitesi çalışıldı. Hücre kültürü çalışmaları, hücre canlılığının nanoparçacık dozuna bağlı bir inhibisyonu olduğunu ve daha yüksek konsantrasyonlarda belirgin sitotoksik etkisi olduğunu gösterdi. Bu çalışmayla çinko oksit nanoparçacıklarının karaciğer kanseri tedavisi için terapötik olarak son derece yüksek potansiyele sahip olduğunu gösterdik. Bu tezin ikinci bölümünde, *Peganum harmala* özütü kullanarak kâğıt bazlı renk dönüştürücüler tasarladık. Bitki özütünün katı haldeki yüksek kuantum verimi nedeniyle, bitki özütünden elde edilen floresan biyomoleküller kristal bazlı (sükroz ve KCl kristalleri) ve selüloz elyaf bazlı (pamuklu pedler ve kurutma kağıtları) matrislere gömüldü. Optik karakterizasyonlar, lif kağıtlarının yüksek kuantum verimliliğine sahip olduğunu gösterdi. Konseptin kanıtı olarak, *P. harmala* özütü gömülü lif kâğıdı bir LED üzerinde renk dönüştürücü olarak kullanıldı ve $21.9 \text{ lm W}_{\text{elect}}^{-1}$ ışımada verimliliğinde mavi renkte ışyan bir cihaz elde edildi. Sonuçlar, bu çevre dostu bitki bazlı malzemelerin, uygun maliyetli ve sürdürülebilir alternatifler olarak şu anda kullanılan renk dönüştürücülerin yerini alabileceğini gösterdi.

Anahtar kelimeler: Bitki aracılı nano-malzemeler; kantaron; üzerlik; çinko oksit nanoparçacıklar; renk dönüştürücü

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LIST OF ABBREVIATIONS

EDX	Energy-dispersive X-ray
FTIR	Fourier transform infrared spectroscopy
LEDs	Light-emitting diodes
QDs	Quantum dots
QY	Quantum yields
PL	Photoluminescence
STEM	Scanning transmission electron microscopy
SEM	Scanning electron microscopy
SSL	Solid-state lighting
XRD	X-ray diffraction
ZnO	Zinc Oxide



Anneme...

Chapter 1

Plant Extracts in Biomedical and Optical Studies

1.1 Introduction

Recently, there has been an increased emphasis on plant study worldwide and a vast body of evidence has been gathered to demonstrate the excellent potential of medicinal plants employed in many traditional treatment approaches. Over the last five years, researchers have studied more than 13,000 plants for biological and optical studies [1].

Plant-derived compounds have shown significant promise in fighting against diseases such as infections and various cancers. These compounds are responsible for a broad spectrum of pharmacological activities in terms of antimicrobial, antidepressant, antioxidant, and anticancer activity. For example, the extract of *Hypericum perforatum* (*St. John's Wort*) has been extensively researched for its antidepressant [2], anti-inflammatory, and antibacterial effects [3]. The active chemicals of this plant extract, hypericin and hyperforin, alter neurotransmitter function and prevent microbial development, demonstrating the medicinal potential of the extracts of *Hypericum perforatum* [4].

With the growing demand for sustainable materials, plant extracts are being integrated into optics to provide unique solutions in fields such as imaging, photodynamic therapy, and advanced lighting systems. Thanks to many semiconductor molecules found in plant extracts, they are employed as natural photosensitizers, fluorescence markers and light-harvesting system components. In the literature, anthocyanins obtained from various berries and flowers are extensively studied for their fluorescence capabilities and have been used in bioimaging and photonic devices [5]. In another study, *Cynara Scolymus*

(Artichoke) extract was employed for the synthesis of silver nanoparticles (AgNPs) as photodynamic therapy (PDT) agents [6].

Within the scope of this thesis, we studied two different plant extracts (*Hypericum perforatum* and *Peganum harmala*) for biomedical and optical applications, respectively. In Chapter 2, we present our study on environmentally friendly green synthesized zinc oxide nanoparticles (ZnO NPs) and their biological activities. Here, anticancer activity results of these nanoparticles against the human liver cancer cell line (Hep-G2) and the antibacterial activity results against *Escherichia coli* and *Staphylococcus aureus* were demonstrated for the first time. In Chapter 3, to create a sustainable and energy-efficient solution for lighting technologies, we studied and presented high-quantum-yield fluorescent *Peganum harmala* extract wrapped into solid crystal and cellulose-based matrices and their LED application as a color converter for the first time. Finally, in Chapter 4, we conclude our two studies and discuss their potential future applications.

Chapter 2

Eco-Friendly Synthesis of Zinc Oxide Nanoparticles for Enhanced Anti-cancer and Anti-bacterial Activity

2.1 Introduction

2.1.1 Nanotechnology and Nanoparticles

Nanotechnology is an interdisciplinary field of science and engineering that employs materials at the atomic, molecular, and supramolecular levels, which generally range from 1 to 100 nanometers. Materials at this size display physical, chemical, and biological characteristics that differ from their bulk counterparts. This leading technology is transforming several areas, including electronics, environmental science, energy, and healthcare [7]. Recently, nanotechnology attracted significant attention in the biomedical and biotechnology fields because of its potential to develop new therapeutic approaches and diagnostic instruments.

Nanoparticles (NPs), a fundamental component of nanotechnology, are defined as microscopic particles with dimensions ranging from 1 to 100 nm in size. Their exceptionally high surface area-to-volume ratio and unique size render them highly suitable for diverse applications [8]. These nanoscale materials exhibit distinctive characteristics, including enhanced chemical reactivity, tunable optical properties, high solubility, and improved therapeutic efficacy while limiting the adverse effects of the drugs, positioning them as promising candidates for advanced applications in medicine and biotechnology [8-9]. For this purpose, some nanoparticles, such as liposomes, polymeric nanoparticles, and metallic nanoparticles (such as gold and silver) are frequently tailored

for drug delivery, diagnostic imaging, antibacterial studies, and cancer treatment [10], while quantum dots and iron oxide nanoparticles are utilized as contrast agents in imaging methods, providing improved resolution and sensitivity in diagnostic applications [11]. Moreover, in the realm of biotechnology, nanoparticles contribute to innovations in biosensors, gene therapy, and tissue engineering. Biosensors based on nanoparticles can detect specific biological molecules at extremely low concentrations, which is critical for early disease diagnosis and monitoring [12]. Moreover, nanoparticles have been employed to deliver genetic material in gene therapy, offering new possibilities in the treatment of genetic disorders [13].

2.1.2 Methods of Nanoparticle Synthesis

The synthesis of nanoparticles can be mainly classified into two categories as top-down (physical methods) and bottom-up approaches (chemical & green synthesis method). Each process has its merits, but among them green synthesis has gained popularity thanks to its environmentally-friendly nature and its sustainability.

2.1.2.1 Physical Methods of Nanoparticle Synthesis

Nanoparticles are produced using physical procedures that use mechanical or thermal energy. Some popular physical approaches are ball milling, laser ablation and Physical vapor deposition. Among them, ball milling is a process for grinding bulk materials into nanosized particles using mechanical force. The fundamental benefit of this technique is the synthesis of nanoparticles without the use of hazardous chemicals, although it frequently requires significant energy and specialized equipment [14]. On the other hand, laser ablation involves irradiating a solid material with a powerful laser, which causes the material to evaporate and condense into nanoparticles. High purity is provided by this method, while it uses a lot of energy and sophisticated technology [15]. The last method known as physical vapor deposition (PVD) is a process of vaporizing a substance and letting it condense into nanoparticles. Despite its capacity to generate precisely specified particles, this approach is expensive and not scalable for use in industrial setting [16].

2.1.2.2. Chemical Methods of Nanoparticle Synthesis

Chemical approaches involve reactions in a solution that result in the formation of nanoparticles. These techniques are classified as chemical reduction, sol-gel process and

microemulsion techniques. Among them, chemical reduction is the process that metallic nanoparticles are formed by reducing metal salts in the presence of reducing chemicals such as sodium borohydride or hydrazine. While this procedure is effective, it frequently requires the use of harmful chemicals, which can pose environmental and health risks [17]. Other method is the sol-gel process includes transitioning a system from a liquid "sol" (a colloidal dispersion of particles) to a solid "gel" phase. Sol-gel methods are utilized to manufacture oxide nanoparticles; nevertheless, they can include dangerous solvents and by-products [18]. The last chemical method is the microemulsion technique where nanoparticles are generated when precursor materials react in a microemulsion including water, oil, and surfactant. While this strategy can provide effective size control, the utilized surfactants are frequently hazardous to the environment [19].

2.1.2.3. Green Synthesis Method of Nanoparticle Synthesis

Green synthesis is a growing field of nanoparticle synthesis where natural sources such as plants, bacteria, fungus, and algae are used as reducing and capping agents in nanoparticle production [20]. Among them, plant extracts gain popularity for nanoparticle synthesis thanks to phytochemicals such as flavonoids, terpenoids, and polyphenols that they include. These phytochemicals have a significant role in the conversion of metal ions into nanoparticles.

2.2.3.1. Advantages of Green Synthesis

The green synthesis method possesses many advantages compared to the physical and chemical methods offering benefits such as eco-friendliness, biocompatibility, cost-effectiveness, simplicity, and scalability. Among them, the eco-friendliness nature of this method helps to reduce harmful agents and solvents as well as lowering the amount of hazardous by-products. This is consistent with the concepts of green chemistry, assisting to reduce carbon footprint. In addition, the biocompatibility of this method is enhanced by the presence of natural capping agents, making them especially valuable in biomedical applications like drug delivery and tissue engineering [21]. Another advantage of this method is its cost-effectiveness since the green synthesis frequently uses easily accessible and affordable biological components, making it more cost-effective than standard approaches that need pricey chemicals and equipment [22]. Lastly, simplicity and scalability of this method are noteworthy, as green synthesis is often easier and more straightforward, with most reactions taking place at normal temperature and pressure. This

makes it easy to scale up for industrial applications without the need for complicated apparatus [23].

2.2.3.2 Green Synthesis Using Plant Extracts

Plant extract-mediated nanoparticle synthesis is one of the most promising green synthesis techniques. Plants like *Hypericum perforatum* (St. John's Wort), *Azadirachta indica* (Neem), and *Camellia sinensis* (Green Tea) have been extensively investigated for their capacity to decrease metal ions and stabilize the resultant nanoparticles [24]. These extracts include bioactive chemicals that reduce metal precursors such as silver nitrate or zinc acetate, resulting in metallic nanoparticles. The phytochemicals in the plant extract also work as natural capping agents, preventing nanoparticle aggregation and stabilizing them in the reaction [25]. In a study reported by Sharie *et. al.*, in the formation of zinc oxide nanoparticles (ZnO NPs) were obtained using *Hypericum triquetrifolium* extract. In this process, a dual function was performed and it both reduced zinc ions and stabilized the ZnO NPs. Then researchers demonstrated the use of these nanoparticles in both antibacterial and anticancer studies [26].

2.1.3 Zinc Oxide Nanoparticles

Zinc oxide nanoparticles (ZnO NPs) are one of the mostly studied metal oxide nanoparticles because of their distinct structural, physical, and chemical characteristics. They reveal hexagonal wurtzite crystal structure which is the most thermodynamically stable form at ambient temperatures. This structure consists of tetrahedral coordination of zinc (Zn^{2+}) and oxygen (O^{2-}) ions, resulting in a non-centrosymmetric polar structure. When reduced to the nanoscale, this polarity and the high surface-to-volume ratio of nanoparticles significantly affect the physical and chemical characteristics of ZnO NPs [27]. ZnO NPs are direct wide-bandgap semiconductors with a bandgap energy of around 3.0 eV. This broad bandgap enables ZnO nanoparticles to have an excellent optical transparency in the visible spectrum and notable ultraviolet (UV) light absorption [28]. These characteristics make ZnO NPs useful for UV-blocking and photocatalytic applications. Besides, ZnO NPs have unusual optical characteristics, such as high exciton binding energy (about 60 meV), making them ideal for light-emitting devices and optoelectronic applications. When activated by UV radiation, ZnO nanoparticles generate fluorescence in the visible area, making them valuable for imaging and sensing applications [29]. They additionally have considerable catalytic characteristics due to

their large surface area and capacity to adsorb molecules, which make them more reactive in many chemical processes, particularly in elimination of pollutants and organic compound oxidation [30]. Moreover, thanks to their non-centrosymmetric nature and piezoelectric properties, ZnO NPs can create electric charge when they are physically deformed. Thanks to these properties, they are also preferred in energy harvesting devices [31]. In addition to their very important optical features, ZnO NPs also reveal crucial biomedical properties. ZnO NPs produce reactive oxygen species (ROS), including hydrogen peroxide (H_2O_2), superoxide ions (O_2^-), and hydroxyl radicals ($\bullet\text{OH}$), which trigger oxidative stress in bacterial cells and cell death [32]. This characteristic is extremely useful in medical and environmental applications.

2.1.4 *Hypericum perforatum* as a Reducing and Capping Agent

Hypericum perforatum also known as *St. John's Wort*, is a medicinal plant widely recognized for its various pharmacological effects, including its usage as an antidepressant, anti-inflammatory and wound healing agent. [33]. *Hypericum perforatum* has recently attracted attention in nanotechnology in green nanoparticle production thanks to its diverse phytochemical, which includes many significant bioactive chemicals that can operate as natural reducing agents. These phytochemicals, including flavonoids [34], phenolic acids, tannins, and terpenoids, have been found to reduce metal ions to metal during the nanoparticle synthesis, providing an eco-friendly alternative to standard chemical methods [35]. In the literature, it is reported that major flavonoids found in *Hypericum perforatum* are quercetin, hyperoside, and rutin. These chemicals have high antioxidant characteristics and can contribute electrons that reduce metal ions like zinc (Zn^{2+}) and silver (Ag^+) into nanoparticles [36]. Another reported bioactive chemical group found in this plant caffeic acid and chlorogenic acid, they are members of phenolic acids, and their strong potential has been shown in the literature [37]. This happens by the binding of these bioactive molecules to metal ions and facilitating them into particles at nanoscale [38]. Additionally, tannins, which are polyphenolic substances, induce the reduction of nanoparticles similar to phenolic acids [39]. Finally, terpenoids are volatile substances that are responsible for the reduction by transferring electrons to metal ions, transforming them into reduced nanoparticles. Terpenoids also have a role in the capping process of the nanoparticles by stabilizing nanoparticles and preventing agglomeration [40].

2.2 Materials and Methods

2.2.1 Materials

Zinc nitrate hexahydrate ($\text{Zn}(\text{NO}_3)_2 \cdot 6 \text{H}_2\text{O}$) (Sigma-Aldrich)

Sodium hydroxide (NaOH) (Sigma-Aldrich)

RPMI-1640

Fetal Bovine Serum (FBS)

Penicillin-Streptomycin (Pen-Strep)

Phosphate -Buffered Saline (PBS)

Trypsin

MTT reagent (ROTH)

2.2.2 Collection and Extraction of the *Hypericum perforatum* Extract

H. perforatum were collected from Sivas, Türkiye. Prior to the extract preparation, the plant was washed, dried and the flowers were grounded into fine powder through an electric grinder. Then, 20 mL of ethanol was added onto 0.4 g of this powder. Right after the addition of ethanol, a red color change in the solution was observed visually. The solution was mixed on a magnetic stirrer at 78 °C for 30 min. At the end of the reaction, the mixture was transferred to falcon tubes and centrifuged at 10.000 rpm for 20 min. The supernatant was transferred to another falcon and the extract was firstly filtered through Whatman filter paper no. 1. For the further cleaning, a 0.45 µm PTFE filter was used and the obtained extract was stored in a refrigerator at 4 °C.

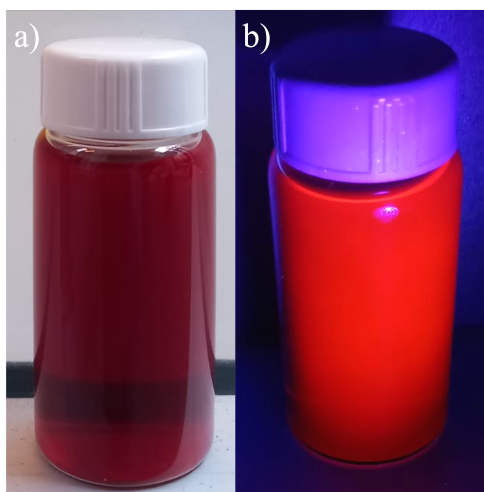


Figure 2. 1 a) The images of *H. perforatum* extract in ethanol under daylight, b) UV-light.

2.2.3 Green Synthesis of *Hypericum perforatum* Extract Mediated Zinc Oxide Nanoparticles (ZnO NPs)

For the green synthesis of zinc oxide nanoparticles, we used zinc nitrate solution as the zinc precursor and *H. perforatum* extract as a reducing agent. In the literature, there are many studies investigating the temperature and pH effect on the green synthesis of ZnO NPs with various plants [41-43]. However, as far as we know there is not any study gating UV exposure effect on ZnO NP synthesis. In the scope of this thesis, we investigated UV irradiation effect on the ZnO NP synthesis process in addition to temperature and pH change. All the experimental groups and the synthesis parameters were given in **Table 2.1**.

Table 2. 1 Experimental Groups and Parameters used in ZnO Syntheses.

	Group numbers	pH adjustment	Final reaction pH	Amount of the extract	Amount of the zinc source	Concentration of NaOH used for pH adjustment	Temperature	Calcination time and temperature
UV (+) Temperature (-)	ZnO 6	-	Reaction pH	5 mL	15 mL (1M)	-	Room temperature (RT)	3 h at 400 °C
	ZnO 11	+	8-9	5 mL	15 mL (1M)	13 mL (1M) NaOH	Room temperature (RT)	3 h at 400 °C
	ZnO 12	+	12-14			1 mL (10 M) NaOH		
UV (-) Temperature (+)	ZnO 14	-	Reaction pH	5 mL	15 mL (1M)	-	110 °C	3 h at 400 °C
	ZnO 10	+	8-9	5 mL	15 mL (1M)	5 mL (1M) NaOH	110 °C	3 h at 400 °C

UV (+) Temperature (+)	ZnO 15	+	8-9	5 mL	15 mL (1M)	1 mL (10M) NaOH	110 °C	3 h at 400 °C
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Here, we systematically studied the ZnO NP synthesis. First, we applied only UV irradiation (without temperature) together with and without pH change (pH 7, pH 8-9, and pH 12-14), then we applied temperature (without UV) with and without pH change (pH 7, pH 8-9), and finally we exposed the reaction all of them (UV, pH change and temperature). Details related to each procedure were discussed below.

ZnO 6, 11 and 12 (UV irradiation with/ without pH adjustment): For the UV irradiation without pH change group (ZnO 6), 5 mL of the extract was mixed with 15 ml of 1M zinc nitrate hexahydrate ($\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$) (Sigma-Aldrich) in water and mixed on a magnetic stirrer at room temperature (RT). Here, the reaction pH was approximately pH 7. For the UV irradiation with pH change group, we studied additional two different pH values as pH 8-9 (ZnO 11) and pH 12-14 (ZnO 12). In order to set solution pH to values, first we followed the same procedure of ZnO 6. However, unlike ZnO 6, after mixing the solution, we gradually added 1 mL of 1M NaOH and 13 mL of 10M NaOH dropwise to obtain ZnO 11 and ZnO 12, respectively. In UV applied groups, a UV lamp emitting at 254 nm was placed close to the mixture on the magnetic stirrer and UV light was applied directly onto the reaction solution for 1 h. Once the reaction was complete, cleaning procedure was carried on. For this purpose, first, the mixture was centrifuged at 10.000 rpm for 20 min and the supernatant was discarded. The pellet was placed into an oven at 50 °C overnight. The dried material was then ground into fine powder in a mortar and calcinated for 3 h at 400 °C to remove impurities. The annealed powder was stored for further experiments. Simultaneously, same steps were repeated without adjusting the pH of the solution in the ZnO 6.

ZnO 10 and ZnO 14 (Temperature-mediated with/ without pH adjustment): For the temperature-mediated and pH adjusted group (ZnO 10), first, 5 mL of the extract was mixed with 15 ml of 1 M zinc nitrate hexahydrate ($\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$) (Sigma-Aldrich) in water and mixed on a magnetic stirrer at 110 °C. Then, 5 mL of (1 M) sodium hydroxide (NaOH) was added into the solution dropwise to adjust the pH of the solution to 8-9 and the mixture was stirred for 1h. Once the reaction was complete, the cleaning procedure

was carried on. For this purpose, first, the mixture was centrifuged at 10000 rpm for 20 min and the supernatant was discarded. The pellet was placed into an oven at 50 °C overnight. The dried material was then ground into fine powder in a mortar and calcinated for 3 h at 400 °C to remove impurities. After subsequent steps of cleaning, drying, grinding, and calcination, white powder of ZnO-NPs was obtained. The annealed powder was stored for further experiments. Simultaneously, these steps were repeated without adjusting the pH of the solution to obtain ZnO 14 sample. It is noteworthy to mention that UV-lamp was not used in these groups.

ZnO 15 (Temperature, UV, and pH adjustment): Finally, to investigate combined effect of all parameters, ZnO 15 was synthesized under UV exposure, temperature, and pH adjustment. For this purpose, 5 mL of the extract was mixed with 15 ml of 1M zinc nitrate hexahydrate ($\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$) (Sigma-Aldrich) in water and mixed on a magnetic stirrer at 110 °C. Next, 1 mL of 10 M sodium hydroxide (NaOH) was added into the solution dropwise to adjust the solution pH to 8-9. A UV lamp emitting at 254 nm was placed close to the mixture on the magnetic stirrer and UV light was applied directly onto the reaction solution for 1 h. Once the reaction was complete, cleaning procedure was carried out. For this purpose, first, the mixture was centrifuged at 10.000 rpm for 20 min and the supernatant was discarded. The pellet was placed into an oven at 50 °C overnight. The dried material was then ground into fine powder in a mortar and calcinated for 3 h at 400 °C to remove impurities. After subsequent steps of cleaning, drying, grinding, and calcination, white powder of ZnO NPs was obtained. The annealed powder was stored for further experiments.

2.2.4 Characterization of Zinc-Oxide Nanoparticles

The physiochemical properties of the green synthesized ZnO-NPs were characterized by UV spectroscopy, X-ray diffraction (XRD), scanning transmission electron microscopy (STEM), scanning electron microscopy (SEM), and energy-dispersive X-ray (EDX) analysis.

2.2.4.1 Optical Characterization

Absorbance spectra of liquid *H. perforatum* extract and solid ZnO solid nanoparticles were measured using a Thermo Genesys 10S UV-vis spectrophotometer between 300-700 nm wavelengths with an interval of 1 nm. For the measurement of liquid *H.*

perforatum extract, sample was added to the ethanol-filled quartz cuvettes while solid ZnO NPs were spread on the glass using double-sided tape and absorbance data were recorded as arbitrary units (a. u.).

The photoluminescence (PL) spectra of liquid *H. perforatum* extract and solid ZnO NPs were measured by Agilent-Cary Eclipse fluorescence spectrophotometer at 400-700 nm range with an interval of 1 nm wavelengths. The extract was added to the ethanol-filled quartz cuvettes while solid ZnO NPs were spread on the glass using double-sided tape. Photoluminescence intensity data were collected in arbitrary units (a. u.).

2.2.4.2 Structural and Chemical Characterization

The size and structure of the ZnO NPs were examined using Zeiss Gemini scanning electron microscope (SEM) for all ZnO NPs groups. Among them, we carried out more detailed investigation for ZnO 11 and ZnO 12 samples. For this aim, we performed scanning transmission electron microscope (STEM) imaging and X-ray diffraction (XRD) analysis. Here, we used XRD characterization to detect the crystal structure of ZnO 11 and ZnO 12 samples. The XRD patterns of the nanoparticles were recorded using a Bruker-D8 Discover X-ray diffractometer. Elemental analysis of the ZnO 11 and ZnO 12 samples were conducted using energy-dispersive X-ray spectroscopy (EDX). After we finished the structural characterization, we carried out cell culture studies. Here, thanks to the good structural properties that they have, we decided to use ZnO 11 and ZnO 12 sample for the anti-cancer and anti-bacterial studies.

2.2.5 Anti-cancer Test of ZnO Nanoparticles against the Human Liver Cancer Cell (Hep-G2)

2.2.5.1 Cell Culture Maintenance

In the cell culture studies, various effects of ZnO 11, ZnO 12, and bare *H. perforatum* extract on human liver cancer cell line Hep-G2 were investigated. Hep-G2 cells were obtained from the German National Resource Center for Biological Material (DSMZ) and cultured in RPMI-1640 supplemented with 10% FBS (fetal bovine serum), 1% L-glutamine and 1% Penicilin. Cells were incubated at 37 °C. in a 5% CO₂ environment. The Hep-G2 cells were passaged in 100 mm dishes with 2.2x10⁶ seeding density and they were detached from surface by trypsinization after reaching %70-80 confluency. Then,

the collected cells were centrifuged at 900 rpm for 5 minutes and the supernatant was removed. The pellet was resuspended in fresh media.

2.2.5.2 MTT Cell Viability Assay

In order to detect the toxic levels of ZnO NPs (ZnO 11 and ZnO 12 sample) and bare *H. perforatum* extract, we performed cell viability assay. Prior to the experiments, 10^4 cells were seeded in each well of the 96 well plate and incubated overnight for the cell attachment. After incubation, the cells were treated with increasing concentrations of the ZnO NPs (ZnO 11 and ZnO 12 sample) (1, 5, 10, 20, 50, 100, 200 $\mu\text{g/ml}$) and *H. perforatum* extract (1, 5, 10, 20, 50, 100, 200, 400 $\mu\text{g/ml}$) and incubated for 48h. Following the incubation, 10 μl MTT reagent was added to each well and incubated for 2h at 37°C and 5% CO_2 . Then, the 96 well plates were centrifuged at 1800 rpm for 10 min and 100 μL of DMSO was added to dissolve precipitated formazan crystals. Then, plates were placed on a shaker for 15 minutes at room temperature in a dark environment. The absorbance was measured at 570 nm by using a spectrophotometer with a Varioskan™ LUX multi-mode microplate reader. The cell proliferation graphs were drawn by using results from the spectrophotometer and IC_{50} values were calculated by using CompuSyn software.

2.2.5.3 Apoptosis Cell Death Assay

To investigate the apoptosis levels induced by different sample groups, Hep-G2 cells were seeded in a 6-well plate with a density of 1×10^6 cells in each well. After overnight incubation, ZnO 11 sample at a concentration of 20.32, and 50 $\mu\text{g/ml}$, ZnO 12 sample at a concentration of 15.77, and 50 $\mu\text{g/ml}$, and *H. perforatum* at a concentration of 50, and 208.1 $\mu\text{g/ml}$ were added onto cells. Plates were incubated at 37°C . in 5% CO_2 for 48h. Afterwards, the cells were washed with PBS and harvested by trypsinization, and the samples were centrifuged at 1700 rpm for 5 minutes at 4°C . The pellets were dissolved in cold PBS and centrifuged at 1700 rpm for 5 minutes at 4°C . After repeating this step twice, the pellets were mixed with 200 μl 1X binding buffer and 2 μl of FITC Annexin-V to detect the early apoptotic cells. Then, samples were incubated for 15 minutes at room temperature in a dark environment and the samples were centrifuged at 1700 rpm at 4°C for 5 minutes. Pellets were dissolved in 200 μl 1X binding buffer and 4 μl of PI was added to detect late apoptotic or necrotic cells. Finally, the cells were analyzed by using BD LSRFortessa (Becton Dickinson) flow cytometry.

2.2.5.4 Scratch Assay

Scratch test, which measures the migration rate of a population of cells on scratched surfaces, was used to assess migratory capacity of Hep-G2 cells following exposure to ZnO NPs and *H. perforatum* extract. For this aim, Hep-G2 cells were seeded in a 6-well culture plate at a density of 5×10^5 cells/well and cultured for 3 days to test their wound healing abilities. The culture media was replaced at regular intervals. After reaching the confluency, a linear scratch was formed on the cell monolayer using a sterile 100- μ L plastic pipette tip and washed with PBS to eliminate cell debris. Cells were treated with a new medium and grown for 16-24 hours. The control group was created using a basal medium. The photograph of each cell was taken using an inverted microscope (Olympus CK40) to determine the distance between adjacent cell layers. The wound regions were analyzed by the Image-J software. The percentage of wound closure was determined using the following formula:

$$\text{Wound closure(\%)} = \frac{(A_0 - A_t)}{A_0} * 100 \quad (2.1)$$

where A_0 is the scratch wound area recorded at hour 0 and A_t is the scratch wound area recorded at time X.

2.2.5.5 Statistical Analyses

Statistical analyses were performed by using CompuSyn and GraphPad Prism 8 software. The comparisons of three sets of MTT assay were done by Dunnet's Multiple Comparison test and the level of significance was set at $P < 0.05$. The comparisons of two sets of cell cycle and apoptosis assays were done by Tukey's Multiple Comparison test, and the level of significance was adjusted at $P < 0.05$.

2.2.6 Antibacterial Activity Study

In order to evaluate antibacterial activity of two ZnO NPs and bare *H. perforatum* extract, *Staphylococcus aureus* and *Escherichia coli* were used as a gram-positive bacteria and gram-negative bacteria respectively. For this aim, agar disc diffusion method was used. Prior to the experiments, bacterial suspensions for each bacterium were prepared with sterile saline (0.9% sodium chloride) and cloudiness was adjusted to a standard solution

of 0.5 McFarland's at a concentration of 1.5×10 CFU/ml. The bacterial suspension was transferred to Mueller-Hinton Agar (MHA) medium in petri dishes and evenly distributed on the medium's surface using a sterile cotton swab. Then blank paper discs containing *H. perforatum* extract and various concentrations of ZnO nanoparticles (0.25, 0.5, 1, 2.5, 5, 10, 20 mg/ml) were placed on the inoculated medium. The plates were incubated at 37 °C for 24 hours and the diameter of the inhibition zone (mm) was investigated.

2.3 Results and Discussion

2.3.1 Photo-physical Properties of *Hypericum perforatum* and ZnO NPs

In this study, visually red-fluorescent extract was obtained by stirring powdered *H. perforatum* extract in ethanol. First, the absorbance and fluorescence spectra of the only extract were recorded to determine its optical properties, and the results are presented in Figure 2.2. The results revealed that *H. perforatum* extract exhibits prominent absorption peaks at 359 nm, 548 nm, and 591 nm, along with red fluorescence under UV light, as illustrated in the real image of the extract in Figure 2.1b.

A study conducted by *Skalkos et al.* demonstrated that the characteristic peaks of the hypericin, which is one of the main components found in *H. perforatum* extract, were around 595 and 640 nm (in ethanol). This finding highlights the similarity between our absorbance spectra and that of *Skalkos et al.* supporting the idea that hypericin is the primary optically active compound in our extract [44]. Moreover, PL measurements revealed that the dominant fluorescence peaks of the extract are at 595 nm and 645 nm, which confirm the literature.

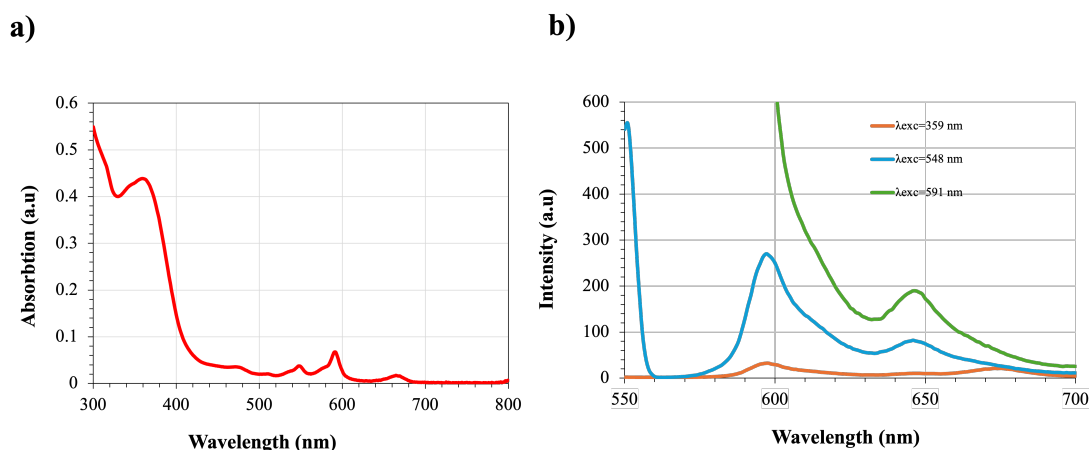


Figure 2. 2 a) Absorbance spectrum, b) Photoluminescence spectrum of *H. perforatum* extract. PL measurements were taken with excitations at 359 nm, 548 nm, and 591 nm excitation wavelengths.

Following the *H. perforatum* extract, absorbance and photoluminescence measurements were conducted for zinc oxide nanoparticles. The absorbance results showed that ZnO 11 sample exhibits a clear peak at 378 nm while ZnO 12 sample exhibits at 375 nm which in agreement with the literature [45]. In PL measurements, we see peaks at 442 nm and 557 nm for both ZnO 11 and ZnO 12. These peaks are also reported in literature and support our results [46].

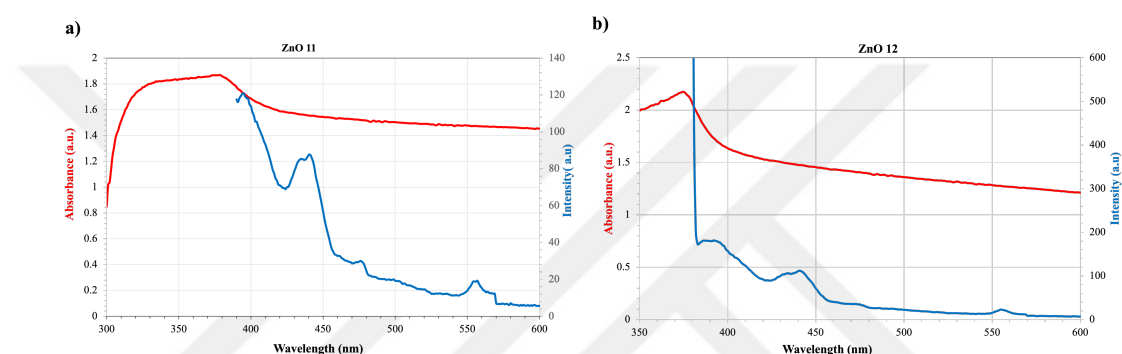


Figure 2. 3 a) Absorbance and photoluminescence spectra of ZnO 11, b) ZnO 12. Excitation wavelengths for photoluminescence measurements were 378 nm for ZnO 11 and 375 nm for ZnO 12.

2.3.2 Chemical and Structural Properties of ZnO NP

While pH and temperature have been extensively studied in the literature [47, 48] the impact of UV exposure remains relatively unexplored. To address this gap, in addition to the effects of pH variation and temperature, we also systematically investigated the UV exposure on ZnO synthesis. For pH variation, two conditions were set: pH 8–9 (with pH adjustment) and pH 7 (without adjustment). In the temperature-applied group, the reaction temperature was increased to 110 °C during the process. SEM images related to these syntheses were presented in Figure 2.4.

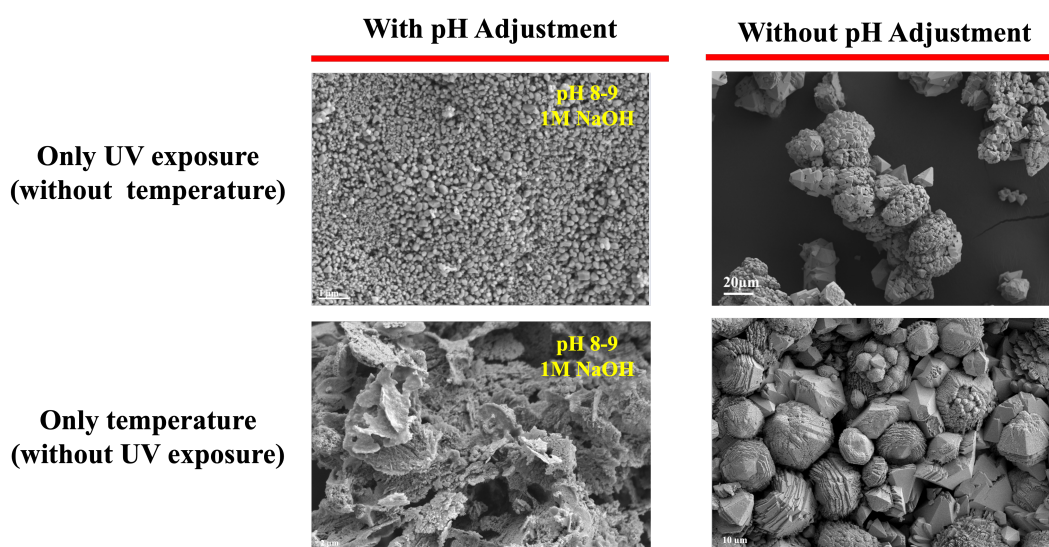


Figure 2. 4 SEM images of only UV exposed ZnO NPs (with/without pH adjustment) and only temperature applied ZnO NPs (with/without pH adjustment).

Figure 2.4 presents SEM images illustrating the morphological differences in ZnO nanoparticles under varying conditions. The upper section compares samples from the UV exposure group with and without pH adjustment, highlighting the structural impact of pH modification. The lower section displays SEM images of the temperature-treated group under similar conditions, demonstrating how temperature and pH adjustment influence ZnO nanoparticle formation. These images provide insights into the interplay between these factors in shaping nanoparticle structure.

When we compare the UV and temperature effects on ZnO formation at pH 8-9 (Figure 2.4, left column), UV exposure induces the formation of smaller nanoparticles in the pH-adjusted groups, while temperature induces sponge-like structure instead of particle. On the other hand, at pH 7 (reaction pH or without pH adjustment), neither UV exposure nor temperature treatment significantly alters particle size. Instead, these factors primarily affect the structure of these crystals (Figure 2.4, right column). Specifically, UV exposure results in large, grape-like agglomerated particles, while temperature treatment induces layer-by-layer structured large particles formation.

When comparing pH adjustment and UV exposure, pH control plays a crucial role in preventing agglomeration in UV-exposed groups. As seen in the upper row of Figure 2.4, UV exposure promotes the formation of small nanoparticles in both pH 8–9 and pH 7 conditions. However, in the reaction pH group (pH 7), these nanoparticles exhibit significant agglomeration.

A different trend was observed in ZnO nanostructures when we compare pH and temperature effect (Figure 2.4, bottom row). Rather than discrete nanoparticles, the temperature-treated samples exhibit a sponge-like structure. Although a particle-like morphology is observed at pH 7 and 110°C, the formations are significantly larger, indicating that temperature primarily influences particle growth and aggregation.

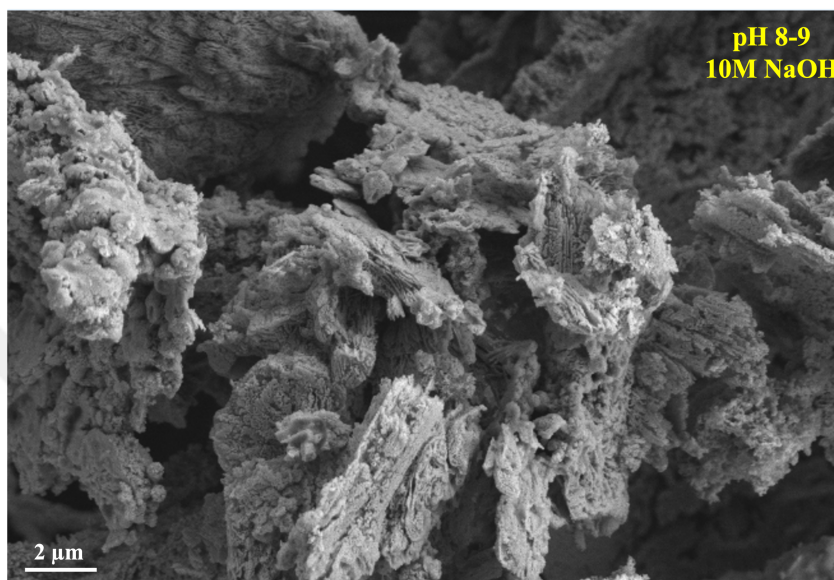


Figure 2. 5 The SEM images of the ZnO structures synthesized with pH adjustment, UV exposure, and temperature application.

Finally, we examined the combined effects of UV and temperature treatment under pH-adjusted conditions, with the corresponding SEM image presented in Figure 2.5. Interestingly, the resulting structure closely resembles that of the temperature-treated, pH-adjusted group (Figure 2.4, bottom left). This finding suggests that when both UV and temperature are applied, the influence of temperature dominates, leading to the formation of a sponge-like structure, overriding the effects of UV exposure.

Based on these findings, since better nanostructure formation was observed, we further explored the effects of higher pH ranges and UV exposure by conducting an additional synthesis at pH 12–14. In this study, ZnO nanostructures synthesized under UV exposure at pH 8–9 was labeled as ZnO 11, while those synthesized at pH 12–14 was labeled as ZnO 12. Their corresponding SEM images are presented in Figure 2.6.

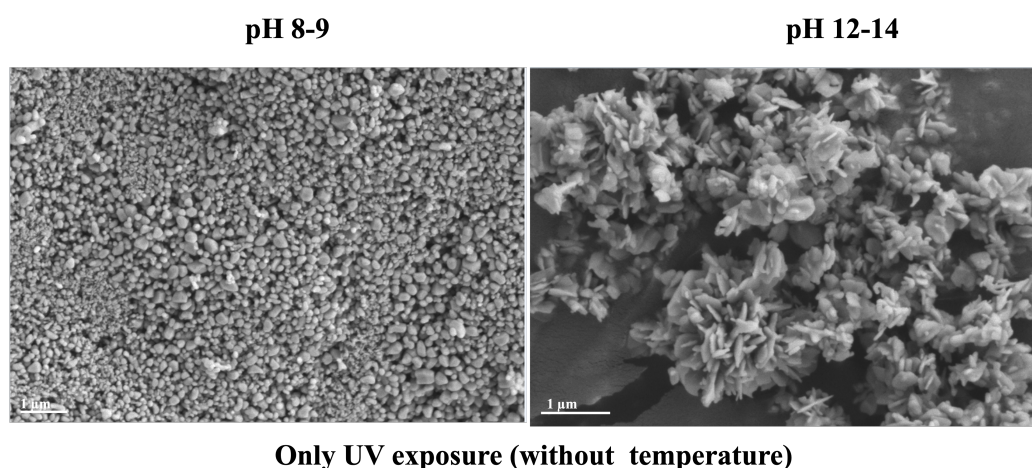


Figure 2. 6 SEM images of ZnO 11, and ZnO 12 sample.

Figure 2.6 reveals that ZnO 11 nanoparticles have a spherical shape, while ZnO 12 have a plate-like structure mixed with ellipsoidal particles. The difference of the shape of ZnO 11, and ZnO 12 sample may be because of the difference pH of the of solution. Average size calculation of ZnO 11 nanoparticles using Image J program exhibited that these nanoparticles show homogenous distribution with an average size of 100-300 nm. However, the size distribution calculation was not possible for ZnO 12. In the literature, a study conducted by *Mahdi Ismail et al.* reports that the pH of the solution affects the properties of the ZnO NPs and high pH conditions are necessary to produce homogeneous particles without agglomeration. Thanks to a good quantity of OH^- ions at high pHs, the ZnO NPs are produced faster compared to those with lower pH [47]. In our study, pH 8-9 (ZnO 11) revealed a better nanoparticle structure and distribution compared to the lower pH 7, which confirms the literature. However, a further increase in pH to 12–14 (ZnO 12) led to a structural transformation, shifting from a spherical morphology to a plate-like structure with localized flower-like agglomerations. This change may be attributed to the influence of UV exposure. Another study performed by *Shaziman et al.* demonstrated the effect of the temperature treatment on the structure of ZnO NP. They revealed that with the increasing reaction temperature, the aggregation of ZnO NPs also increases because of the enhanced frequency of collisions among nucleating atoms during the particle synthesis. In this way, these collisions lead to the dispersion of nucleated atoms, significantly enhancing surface mobility and increasing their reactivity, which helps prevent the formation of dense aggregates. In our temperature-treated group we also see an aggregated sponge-like structure, which confirms the literature [48].

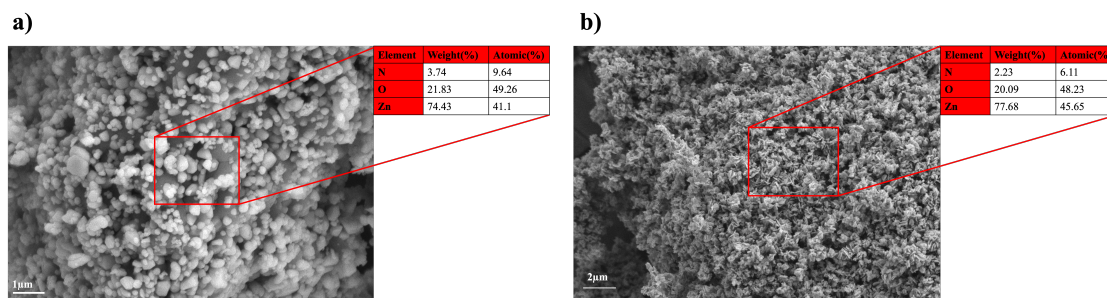


Figure 2. 7 a) SEM images and EDX analysis of ZnO 11, b) ZnO 12 sample.

After the structural characterizations, energy dispersive X-ray (EDX) analysis was conducted to confirm the elemental composition and purity of the synthesized ZnO NPs. The EDX spectrum for the ZnO 11 sample (Figure 2.7a) displayed prominent peaks corresponding to zinc (Zn) and oxygen (O), verifying the successful formation of ZnO. The absence of significant peaks for other elements indicates high purity of the material with minimum contamination. Similarly, the ZnO 12 sample (Figure 2.7b) exhibited distinct Zn and O peaks, with minor variations in peak intensities, suggesting slight differences in the surface properties between the two samples. The elemental weight and atomic percentages derived from the EDX analysis further confirmed the ZnO NPs composition.

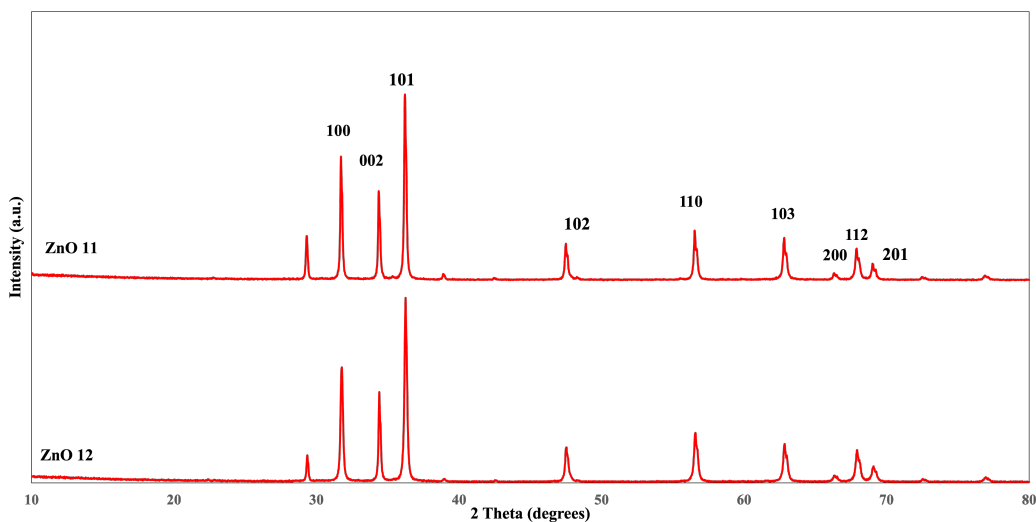


Figure 2. 8 XRD spectrum of ZnO 11 sample (upper), and ZnO 12 sample (bottom).

Finally, the X-ray Diffraction (XRD) spectra of the ZnO 11 (Figure 2.7, upper) and ZnO 12 (Figure 2.7, bottom) samples confirm their crystalline structure, characteristic of hexagonal wurtzite ZnO. The diffraction peaks observed at 2θ values of approximately

31.7°, 34.4°, 36.2°, 47.5°, 56.6°, 62.9°, and 68.0° correspond to the (100), (002), (101), (102), (110), (103), and (112) crystal planes, respectively, these peaks are consistent with the standard diffraction pattern of ZnO, indicating a high degree of crystallinity.

2.3.3 Anticancer Effect of ZnO NP against the Human Liver Cancer Cell (Hep-G2)

In order to investigate the anticancer effect of ZnO 11, ZnO 12 sample and *H. perforatum*, we treated the HepG2 cell line separately with each ZnO 11 (1-200 μ M), ZnO 12 (1-200 μ M), and *H. perforatum* (1-400 μ g/ml) in a dose-dependent manner for 48 hours (Figure 2.9).

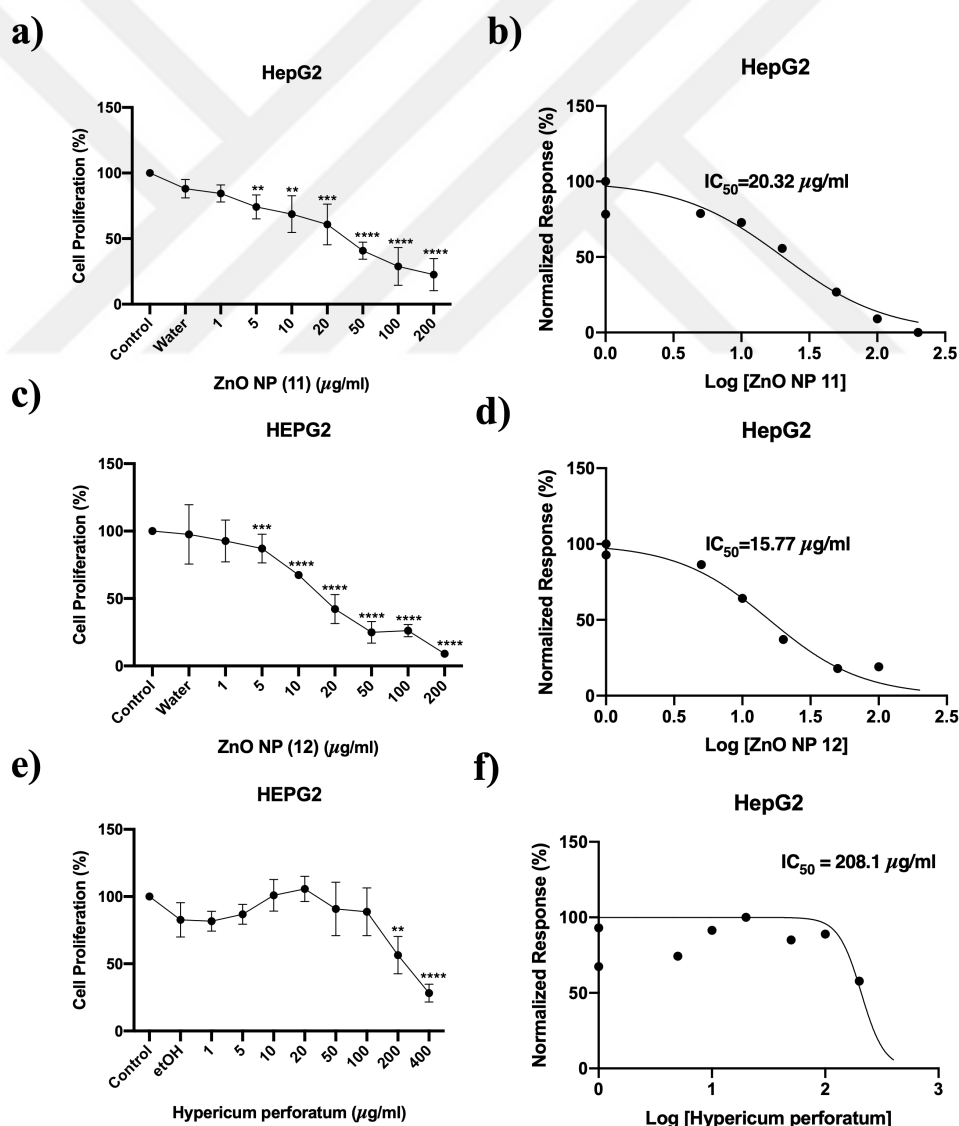


Figure 2. 9 a-b)The cell viability and corresponding IC₅₀ value of Hep-G2 cells after treatment with increasing concentrations of ZnO 11 NP, c-d) ZnO 12 NP and e-f) *Hypericum perforatum* for 48h.

Our results indicate that when the concentration increased, a significant decrease in cell viability was observed compared to the untreated control cells. While a low zinc oxide nanoparticle concentration of 1 µg/ml caused a 15% decrease in cell viability, a significant 80-85 % decrease in cell viability was observed when the highest concentration was applied at 200 µg/ml. Later, *H. perforatum* was used to treat Hep-G2 cells in different concentrations, 1 µg/ml, 5 µg/ml, 10 µg/ml, 20 µg/ml, 50 µg/ml, 100 µg/ml, 200 µg/ml, and 400 µg/ml to investigate the anticancer potency (Figure 2.9e-f). Compared to the untreated control group, an important decline in cell proliferation was observed in the dose boosted groups. Results demonstrated a dose-dependent inhibition of cell viability, with significant cytotoxic effects observed at higher concentrations. The IC₅₀ value was determined to be 20 µg/ml for ZnO 11 sample (Figure 2.9b) and 15.77 µg/ml for ZnO 12, indicating the potential of ZnO NPs as a therapeutic agent for liver cancer treatment. Whereas the IC₅₀ value was determined to be 208.1 µg/ml for *Hypericum perforatum*.

2.3.4 Antibacterial Effect of ZnO NPs and *H. perforatum* against *E. coli* and *S. aureus*

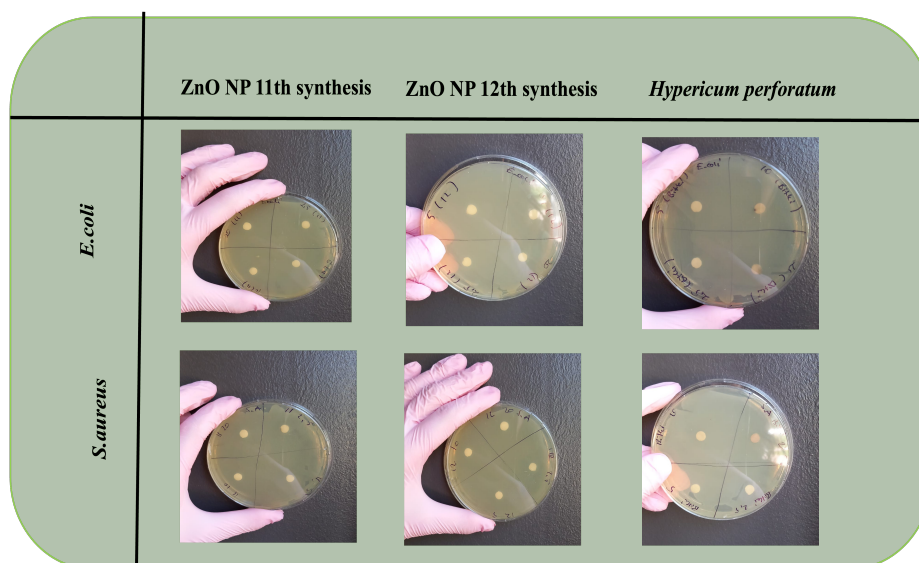


Figure 2. 10 Antibacterial activity of ZnO 11 and ZnO 12 sample and *Hypericum perforatum* on *S. aureus* and *E. coli* respectively.

To evaluate the antibacterial potency of *H. perforatum* extract, ZnO 11 and ZnO 12 nanoparticles, we performed antibacterial test against the *E. coli* (gram-negative bacterium) and *S. aureus* (gram-positive bacterium), results of which are given in Figure 2.10. For this purpose, different concentrations such as 2.5 mg/ml, 5 mg/ml, 10 mg/ml, and 20 mg/ml were studied for ZnO 11 and ZnO 12 nanoparticles and *H. perforatum* extract. As seen in Figure 2.10, no significant inhibition zones were observed in any of the experimental groups.



Chapter 3

Sustainable Next-generation Color Converters from *P. harmala* Seed Extracts for Solid-state Lighting

3.1 Introduction

Solid-state lighting (SSL) based on light-emitting diodes (LEDs) provides high-quality lighting with greater efficiency, reduced energy consumption, and a significantly longer lifetime [49]. Currently, blue LED chip integrated with color-converting materials is used in the SSL technology [50]. Phosphors consisting of rare-earth metal ions are the most extensively utilized material system for generating color-converting films [51]. Although their excellent photoluminescence quantum yields (QY), alternatives are in need owing to (i) the difficulty in modifying their colors, which limits their performance, (ii) supply problems, and (iii) the environmental footprint of mining rare-earth metals [52] that are utilized to produce phosphors. Quantum dots (QDs) have surged forward because they allow easy color-tuning of the LEDs and are less vulnerable to the supply crises among the alternatives [53]. Nevertheless, the efficient QDs are toxic due to their cadmium content while their synthesis is far from being environmentally friendly [54]. Although organic semiconductors could be promising despite their stability issues [55], their syntheses possess a substantial environmental footprint similar to the QDs. In this work, we explore the possibility of using plant extracts as sustainable alternatives to phosphors, QDs, and organic semiconductors, with an emphasis on *Peganum harmala*. Plants have been traditionally used for curing owing to various biomolecules that they have, such as alkaloids, flavonoids, phenols, anthocyanins, *etc.* [56-59] extraction of these molecules has been studied intensively in the literature, mainly for pharmacologic and therapeutic purposes [60]. On the other hand, some of these plants possess autofluorescent biomolecules which absorb the light and reemit at longer wavelengths

[61] This feature enables imaging certain plant parts without tagging with a reporter molecule [60, 61]. However, the potential of these auto fluorescent biomolecules has not been evaluated as alternatives to synthetic fluorescent probes including semiconducting polymers, their nanoparticles, or quantum dots (QDs). Despite their availability, sustainability, eco-friendly nature, bio-compatibility, and low cost [62], a limited number of studies report their use in applications other than pharmacology and biotechnology. These include flexible electronics (e-skins) [63], solar cells [64], and energy storage [65]. For lighting applications, Roy *et al.* [66] synthesized green-emitting graphene quantum dots from plant extracts obtained from neem (*Azadirachta indica*) and fenugreek (*Trigonella foenum-graecum*) and employed them to obtain white LEDs. In another study conducted by Singh and Mishra [67], fluorescent polymer films were prepared using red pomegranate and turmeric extracts to generate white light on a blue LED. In this work, the QYs of the fluorescent molecules in the extract were reported as <10% whereas the QY of the films, which are likely less than the in-solution-QYs due to aggregation effects, were not reported. Therefore, the research efforts need to be directed toward obtaining their efficient solids to use the plant extracts in solid-state lighting (SSL). With this motivation, we studied the potential of water extract of *Peganum harmala*, also known as *Syrian rust* or *African rue*, for utilization in SSL. Phytochemically, this plant is rich in β -carbolines alkaloids such as harmine, harmaline, harmalol, and harman and quinazoline derivatives such as vasicine, vasicinone, and deoxyvasicinone [68-69] and has several applications, particularly for therapeutic purposes such as antibacterial, antifungal and antiviral effects, [70-72] anti-tumour effect [72] and, insecticidal effect [59]. Although its blue-green fluorescence is known, [73] the literature lacks sufficient information about its optical characterizations and their application in SSL. With this motivation, here, we prepared the water extract of *P. harmala* and characterized its optical features. Its quantum yield beyond 75% shows that this extract can be a good candidate for SSL if it can sustain these QYs at reasonable levels in solid form. For this purpose, we prepared solids of *Peganum harmala* by embedding the biomolecules into two crystalline matrices, sucrose and KCl, and into two fibrous matrices, cotton, and paper. Then, we integrated the solid matrix having the highest QY with a UV LED chip to prepare color-converting LEDs.

3.2 Materials and Methods

3.2.1 Materials

Potassium chloride (KCl) (Sigma-Aldrich)

Sucrose (Sigma-Aldrich)

Double distilled water (ddH₂O)

3.2.2 Extraction and Chemical Characterization of *P. harmala*

P. harmala was purchased from a local store in Kayseri, Türkiye. *P. harmala* seeds were ground using a mortar, and then 5 g of this powder was mixed with 50 mL of double distilled water (ddH₂O). The solution was kept dark at room temperature for 24 hours. The mixture was first filtered for cleaning using Whatman filter paper (No. 1). Then, the solution was centrifuged at 5000 rpm for 10 min and filtered using a 0.2 µm cellulose acetate hydrophilic filter (Minisart, Sartorius). The aqueous solution of *P. harmala* seeds was stored at 4 °C for further use in our experiments. The extraction yield of the *P. harmala* was calculated using the following **equation (3.1)**:

$$\text{Extraction yield (\%)} = \frac{W_1}{W_2} \times 100 \quad (3.1)$$

where W_1 represents the dry extract weight (g) after solvent evaporation and W_2 represents the weight (g) of the dry seed power before the extraction.

3.2.3 Fabrication of Fluorescent Solid Composites

3.2.3.1 Preparation of Crystals and Pellets of *P. Harmala*

Prior to the experiments, fresh sucrose and salt stock solutions were prepared. For this purpose, 260 g and 170 g of sucrose and potassium chloride (KCl) were separately dissolved in 500 mL of ddH₂O. Solutions were filtered using a 0.2 µm hydrophilic filter to remove any impurities. For the crystallizations, *P. harmala* extract, stock sucrose or KCl solutions and ddH₂O were mixed at given volumes (Table 3.1) in a polystyrene Petri dish without lid (60 mm). Samples were dried in a fume hood at room temperature.

Table 3. 1 Solutions and Their Volumes Used in the Crystallization Processes.

	Volume of <i>P. harmala</i> extract (mL)	Volume of stock sucrose solution (mL)	Volume of stock KCl solution (mL)	Volume of water (mL)
<i>P. harmala</i> in sucrose crystals	1mL	2 mL	-	2 mL
<i>P. harmala</i> in KCl crystals	1mL	-	2 mL	2 mL
Sucrose crystals (control group)	-	2 mL	-	3 mL
KCl crystals (control group)	-	-	2 mL	3 mL

After the crystals were formed, samples were powdered using a mortar. Sucrose and KCl pellets (monoliths) were prepared by applying high pressure to these powders in a hydraulic press (Specac, Atlas Manual). Briefly, 125 mg of the powders were placed between two stainless steel disks, and a pressure of 0.75 GPa was applied using a hydraulic press for 10 min at room temperature.

3.2.3.2 Preparation of Fluorescent *P. harmala* Cotton and Fiber Paper

For embedding *P. harmala* extract into fibrous cellulose materials, cotton pads (Lure) and fiber papers (Munktell, 67 N grade) were employed. First, small disk-shaped papers were cut at a diameter of ~1 cm from a general-purpose fiber drying paper to prepare paper-based solids. Subsequently, 2 mL of *P. harmala* solution was transferred to a 60 mm polystyrene Petri dish and disk-shaped papers were soaked into this solution and kept for 2 min. Next, papers were removed from the solution and kept in a fume hood until completely dry. For cotton sample preparation, 2 mL of *P. harmala* solution was transferred to a 60 mm polystyrene Petri dish. The cotton pad was completely soaked into this solution and kept in a fume hood until they were completely dry. As control groups, samples were prepared by following the same steps for cotton and paper hosts, except that only double distilled water (ddH₂O) instead of *P. harmala* solution was employed.

The chemical characterization of the phytochemicals in *Peganum harmala* was carried out using a QP2010 gas chromatography with a Thermal Desorption System, TD 20 coupled with Mass Spectroscopy (GC-MS) (Shimadzu, Japan). The ionization voltage was used as 70 eV, and gas chromatography was conducted in the temperature programming mode with a Restek column (0.25 mm, 30 m, 5 MS). The initial column temperature was set at 40 °C and then gradually increased to 100 °C before holding for 1

minute. Subsequently, it was raised to 270 °C and maintained for 5 minutes. The injection port temperature was kept at 280 °C, and the GC-MS interface was also maintained at 280 °C. Sample introduction was carried out using an all-glass injector operating in splitless mode, with a helium carrier gas flow rate of 1.2 mL min⁻¹. Compound identification was achieved by comparing retention times and fragmentation patterns, along with the mass spectra obtained from GC-MS analysis.

3.2.4 Optical and Structural Characterizations

Optical characterization of aqueous *P. harmala* extract was performed by absorption, photoluminescence, and quantum yield measurements. UV-Vis absorption spectrum of *P. harmala* extract was acquired with a UV-1800 UV-Vis spectrophotometer (Shimadzu) between 250 and 700 nm. The photoluminescence (PL) spectrum was recorded with an Agilent-Cary Eclipse fluorescence spectrophotometer at an excitation wavelength of 382 nm. The quantum yield (QY) of the solution was measured using a reference dye, Coumarin 153, which has a quantum yield of 54.2%. Briefly, the absorbance of the *P. harmala* extract and the coumarin 153 dye was acquired. Then, the PL spectra of both extract and dye were measured at the excitation wavelength where both absorbance spectra cross. Using the PL data, the QY of the extract was calculated according to equation (3.2):

$$\phi_{\text{extract}} = \left(\frac{\int S_{\text{extract}}(\lambda) d\lambda}{\int S_{\text{dye}}(\lambda) d\lambda} \right) \times \left(\frac{n_{\text{extract}}}{n_{\text{dye}}} \right)^2 \times \phi_{\text{dye}} \times 100\% \quad (3.2)$$

where ϕ stands for the QY, n corresponds to the refractive index, and S indicates the PL spectrum. Here, the extract is *P. harmala* extract, and the dye is coumarin 153. QYs of the solid samples (sucrose pellet, KCl pellet, cotton, and fiber paper matrices) were measured using a Hamamatsu absolute PL Quantum Yield Spectrometer C11347 system that employs an integrating-sphere ($\lambda_{\text{exc}} = 390$ nm).

Structural characterizations were conducted using fluorescence microscopy, scanning electron microscopy (SEM), and scanning transmission electron microscopy (STEM) to understand the effect of morphological variations on the optical properties. Fluorescence microscopy images were recorded using a Nikon Eclipse Ni fluorescence microscope. Electron microscopy images were taken using ZEISS-Gemini SEM/STEM 300 Scanning Electron Microscopy. SEM images were taken at 3 kV or 5 kV, and before the imaging,

a 5 nm Au layer was sputtered on the sample. Image J program was utilized to measure the sizes of only KCl, only sucrose, KCl including *Peganum harmala* and sucrose including *Peganum harmala* crystal powders obtained from STEM images.

3.2.5 Light-emitting Diode (LED) Application

The paper sample having the highest QY was used for LED measurement. The paper was placed on a commercially available low-power LED having a peak emission wavelength of 400 nm after a small volume of epoxy resin was added onto the LED to fix the sample on the LED. The luminance was recorded using a Hamamatsu integrating sphere and spectrometer. Colorimetric and photometric characterizations were carried out employing in-house written codes.

3.3 Results and Discussion

The green-fluorescent extract used in this study was obtained by brewing the powdered *P. harmala* seeds in double distilled water for 24 h (Figure 3.1a), and the extraction yield was calculated as 17.16% using equation 3.1. Then, the absorbance and fluorescence spectra of the aqueous *P. harmala* extract were examined to reveal the optical properties of the extract (Figure 3.1b).

Results demonstrated that *P. harmala* has a very prominent absorption peak at 365 nm. In the literature, although a couple of studies report the absorption spectra of green synthesized nanoparticles using *P. harmala* extracts as reducing agent [74], there is only one report about the absorption spectrum of *P. harmala* extract in water [75]. Interestingly, the absorbance spectrum reported by *Azizi et al.* [75] has no strong peaks but weaker shoulders around 460 and 640 nm. On the other hand, our extract possesses a clear and strong absorbance peak of around 365 nm, which is similar to the report of *Bhattacharjee et al.* on harmaline [76]. The difference in the spectra between our extract and *Azizi et al.* [75] may stem from different extraction conditions employed. Furthermore, the similarity between our absorbance spectra and that of *Bhattacharjee et al.* [76] indicates that harmaline is the most prominent optically active chemical in the extract.

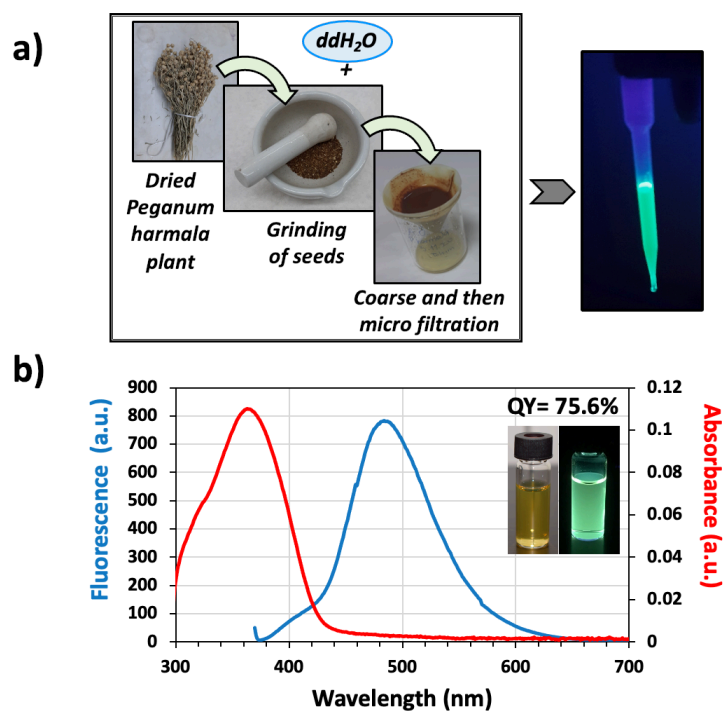


Figure 3. 1 a) Representative image of extraction procedure from *P. harmala* seed. b) Absorbance and fluorescence data of *P. harmala* extract in water. QY data and the photos of *P. harmala* extract in water under daylight and UV light are also shown on the top right side.

Peganum harmala has been reported in the literature as a plant species rich in fluorescent phytochemicals such as harmaline, harmalol, harmine, and norharman, which are β -carboline alkaloids [68]. To identify the phytochemicals found in our aqueous *Peganum harmala* extract, we performed Gas Chromatography-Mass Spectroscopy (GC-MS) analysis (Figure 3.2a-d). Results revealed that the predominant constituents within the *Peganum harmala* seed extract are fatty acids, aldehydes, and alkaloids (Figure 3.2b). Notably, the GC-MS findings highlighted the prevalence of several key compounds, namely harmine (48.59%), 2,3-dihydro-1*H*-2-isopropylcyclopenta[*b*]quinoxaline (17.67%), beta-carboline, 8-methoxy-1-methyl- (11.46%), and 1-ethyl-5-methyl-5-isopropylaminobabaturic acid (4.05%), respectively. Aromatic β -carboline alkaloid (harmine) is well-studied among these naturally occurring alkaloids, and it emits a unique green color under UV light, indicating it might play a significant role in the overall emission of our plant extracts. Furthermore, our analysis identified 8-methoxy-1-methyl-9*H*- β -carboline, an isomer of harmine, comprising 11.46% of the extract. Although photophysical features of this specific molecule is missing in the literature, the presence

of benzene rings strongly indicates a semiconductor nature. Furthermore, a detailed analysis of its chemical structure reveals that it only differs from the autofluorescent molecule harmine by the position of the oxygen. Therefore, we evaluate that this molecule is highly likely an autofluorescent molecule; nevertheless, for a definite experimental proof, isolation of 8-methoxy-1-methyl-9H- β -carboline and its optical characterization are required, which is beyond the scope of this current work.

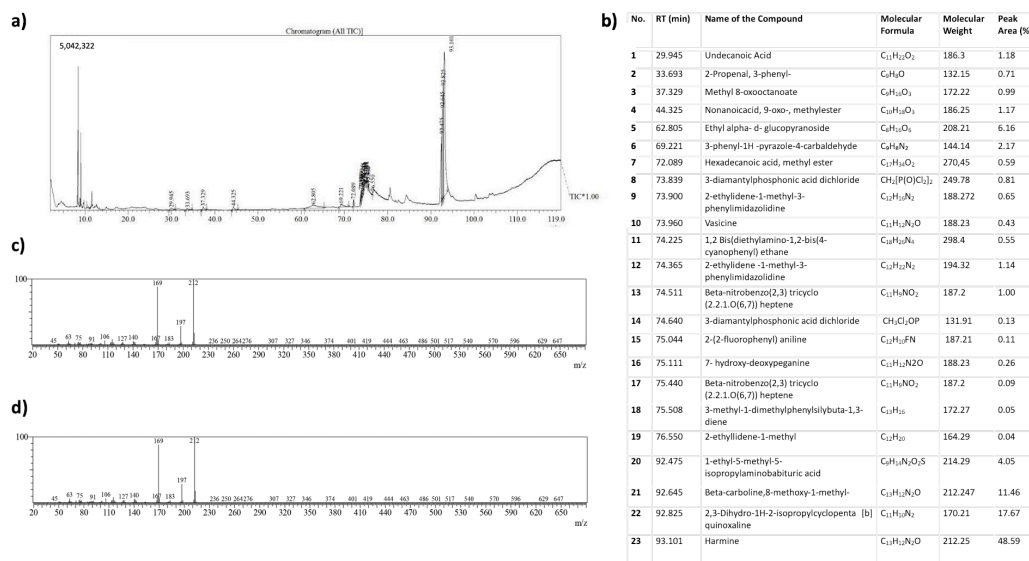


Figure 3. 2 a) GC-MS chromatogram of aqueous extract of whole plant extract of *P. harmala*, b) Phytochemicals identified in *P. Harmala* seed extract, c,d) Mass spectra of harmine and beta-carboline 8-methoxy -1-methyl identified by GC-MS, respectively.

It has been previously reported in the literature that the seeds of *P. harmala* emit light at 473 nm which is largely attributed to its harmalol component [77]. However, more than one molecule emitting at a similar wavelength range generally contributes to the final emission color in plant extracts. To characterize the emission profile of our extract, we performed a photoluminescence (PL) measurement, and the results showed that our extract has a fluorescence peak at 490 nm when it is excited at 382 nm (Figure 3.1 b). Here, similar to the absorbance spectra, there is a strong similarity between the PL of our extract and the harmaline PL spectrum reported by *Bhattacharjee et al.* [76] which further supports our previous conclusion on the dominance of harmaline throughout the extract. However, since other alkaloids in the plant's structure carry a beta-carboline ring structure, we believe these biomolecules also contribute to the emission profile of our extract.

Quantum yield is one of the main parameters for successful implementation of a color converter in SSL applications. A decrease in quantum yield during the transition from liquid to solid state is a significant problem avoiding the use of various fluorescent materials in SSL. To overcome this problem, our group previously demonstrated that when inorganic and organic nanoparticles are incorporated into crystalline matrices, the QYs and the emission stability of these fluorophores improve [78-79] making these nanomaterials attractive for SSL applications. However, the distribution of plant-based fluorophores and their optical properties in these matrices have not been studied previously.

In order to study plant-based solid surfaces, first, we measured the QY of the *P. harmala* extract and found it as 75.6%. Such a high value makes it comparable to the levels that inorganic, toxic quantum dots or some fluorescent polymers provide [80-81]. In the literature, *Hidalgo et al.* [82] reported the QYs of norharman, harmane, harmalol, and harmol, which are the chemical compounds in *P. harmala* extract, as 16%, 17%, 39%, and 49%, respectively. These values were significantly lower than our QY results. At this point, it is worth highlighting that the QY of the extracts may be affected by the extraction procedure (e.g. solvent type, method, time, etc.) and purification processes, potentially leading to lower QYs in the study of *Hidalgo et al.* than the one we measured.

To transfer our *P. harmala* extracts to the solid-state, we first approached the *P. harmala* extract crystallization in saturated sucrose and potassium chloride (KCl) solutions. Obtained crystal structures and their preparation details are provided in Figure 3.3 and Table 3.1, respectively.

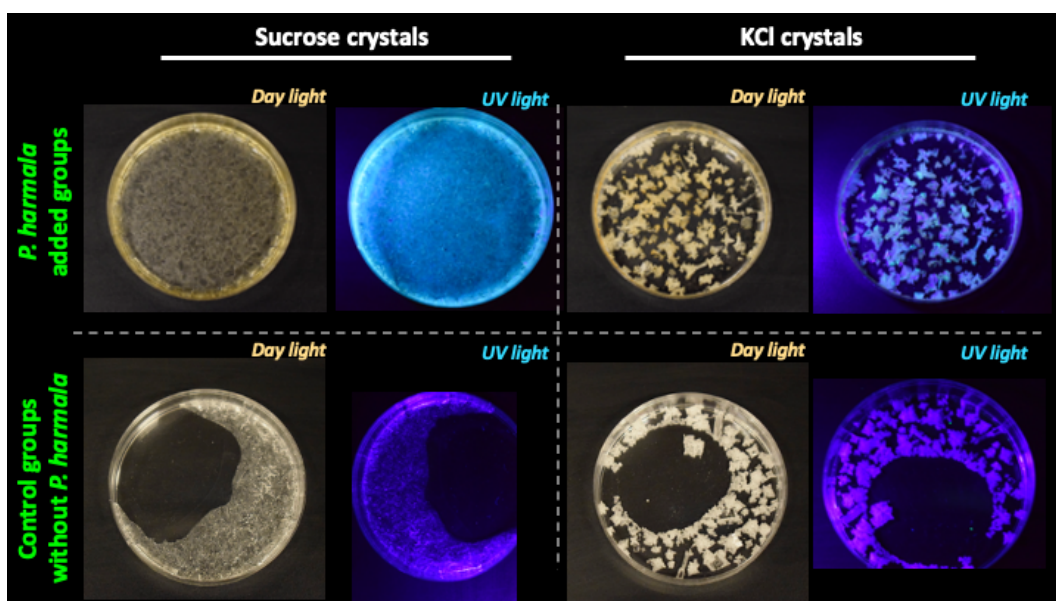


Figure 3. 3 Images of sucrose and KCl crystals with and without *P. harmala* under ambient lighting and UV illumination.

As seen in Figure 3.3 and magnified images of the crystals provided in Figure 3.4, KCl crystals tend to form small crystal grains separately and *P. harmala* extract is localized in some parts of these grains. However, as opposed to KCl crystal, sucrose formed a large and continuous one piece of crystal and covered the Petri dish surface relatively homogeneously. Furthermore, the fluorescent molecules of the *P. harmala* extract are distributed more homogeneously within the whole sucrose crystal structure instead of localizing in some parts. The strong ionic forces in salt solution might cause the aggregation of luminescent molecules and prevent a homogenous distribution of the extract within the salt matrix. Additionally, although we used the same total volume (5 mL, Table 3.1) in both the control and *P. harmala* groups, we observed that *P. harmala* including groups covered a larger area on the dish surface than the control groups (Figure 3.3). The lowered cohesive forces and, thus, the lowered surface tension of water in the presence of extract have contributed to this observation.

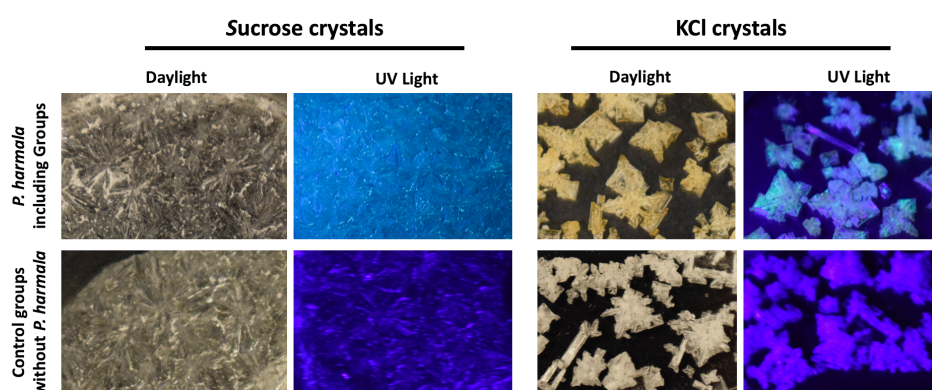


Figure 3. 4 Images of sucrose and KCl crystals with and without *P. harmala* extract.

Although *P. harmala* extract is transferred to the solid state in these crystals, the fabrication of a pellet (monolith), which includes homogeneously distributed fluorescent biomolecules and allows for easy handling, is crucial for LED studies. For this purpose, first, we ground these sucrose- and KCl-based crystals into powder forms using a mortar. Then, we obtained the pellets having a diameter of ~1 cm by applying high pressure to these powders. The images of the powders and monoliths under daylight and UV light are presented in Figure 3.5.

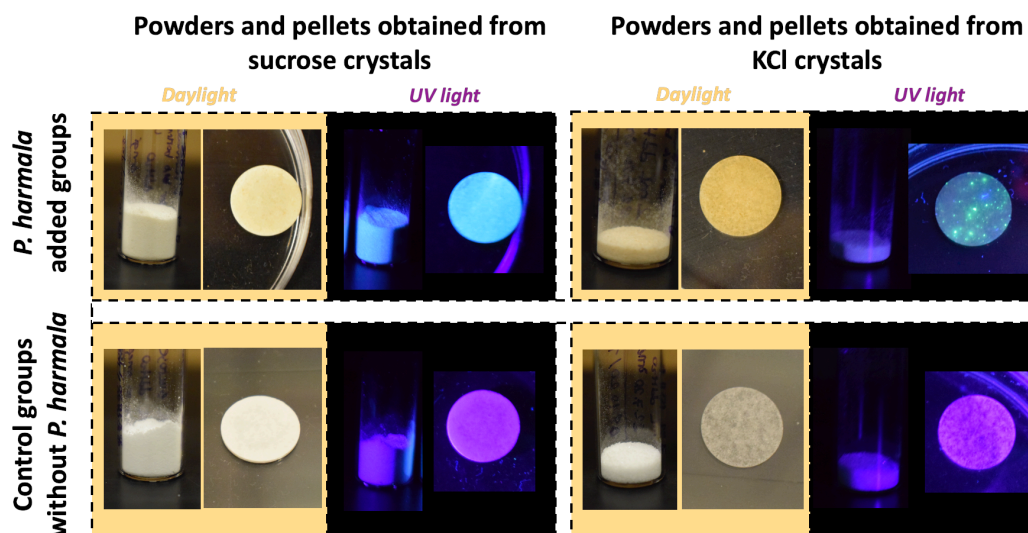


Figure 3. 5 Images of powders obtained from ground crystals and solid pellet structures obtained from powders under daylight and UV light. For sucrose and KCl, control groups and *P. harmala* incorporated groups are presented together.

Consistent with Figure 3.3, green fluorophores aggregated at specific locations of the KCl pellet and represented a nonhomogeneous distribution. However, the homogenous distribution of the fluorophores which causes homogenous greenish emission was observed within the sucrose pellets (Figure 3.5, left-top). In addition to the crystalline matrices, we also investigated two different fibrous matrices. Using these materials, first, we aimed to avoid the aggregation of the fluorescent molecules, which is more likely to occur during drying and crystal formation. Secondly, the random distribution of *P. harmala* extract in different fiber structures and the effect of this distribution on the optical features were studied. In accordance with this, here we employed cellulose, which is one of the most abundant sustainable, renewable, and biocompatible natural polymers in the biosphere. Besides, thanks to their chemical structure, cellulose-based materials are known as exceptional adsorbants [83].

Considering their outstanding features, we immersed the fluorescent *P. harmala* extract into cellulose-based materials and compared them with our crystal-based host matrices. We chose cotton pad and fibrous drying paper as cellulose-based materials because of their easy accessibility and low cost. Briefly, cotton and fiber papers were soaked into *P. harmala* extract, and then they were dried (Figure 3.6). Although some orange shade was observed in some parts of the *P. harmala*-embedded cotton and paper in the daylight images, a homogenous emission was obtained under UV illumination.

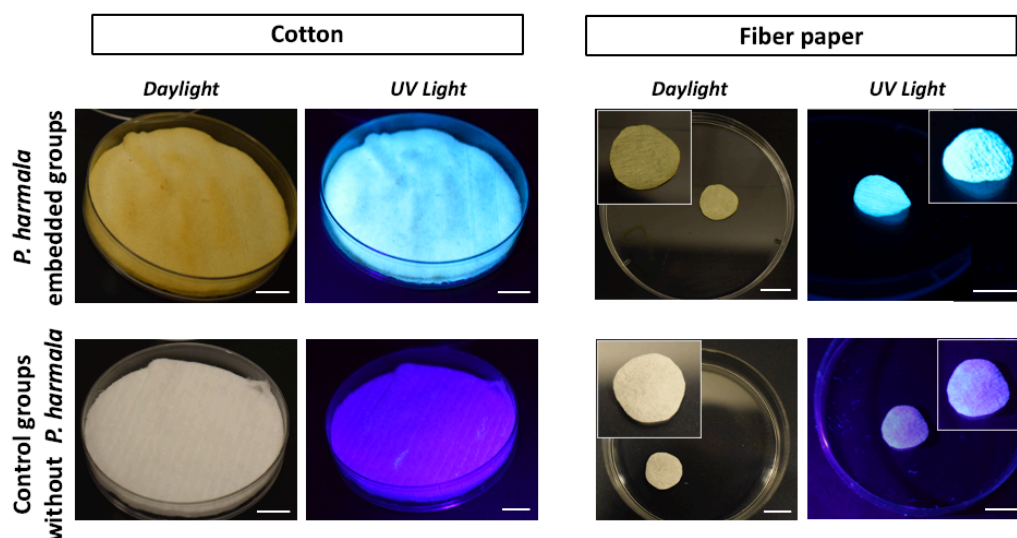


Figure 3. 6 Images of cotton and fiber paper groups with and without *P. harmala* under daylight and UV light. Insets demonstrate the magnified pictures of the fiber paper groups. Scale bars: 1 cm.

We also characterized the *P. harmala* embedded sucrose crystal, KCl crystal, cotton, and fibrous paper under a fluorescence microscope and scanning electron microscope (SEM) to understand the structure-extract distribution relation in detail (Figure 3.7). The sucrose pellet showed a cloudy structure with mostly homogeneous emission in the fluorescence microscope images (Figure 3.7a). On the other hand, the KCl pellet was not cloudy, and the details were distinguishable. However, the green-emitting areas were nonhomogeneous across the monolith compared to the sucrose pellet (Figure 3.7b). Small spot-like structures were observed when we looked closer at both sucrose and KCl monoliths. These structures were more prominent in the sucrose monoliths. Interestingly, the borders of these structures are fluorescent instead of their core, as indicated by the red arrows in Figure 3.7a and b. This reveals that *P. harmala* extract surrounds the sucrose and salt molecules. In addition, the distribution and interconnection of these bead-like structures are more homogenous in the sucrose monolith than KCl monolith. As seen from SEM images given in Figure 3.7e and f both sucrose and KCl monoliths have smooth surfaces and linear lines (shown with white arrows) occurring because of the applied pressure between two steel cylinders in the hydraulic press to obtain the monolith structure. On the other hand, in the magnified images given in the insets, we observed small grape-like structures coming together, which supports our observations in Figure 3.5a and b.

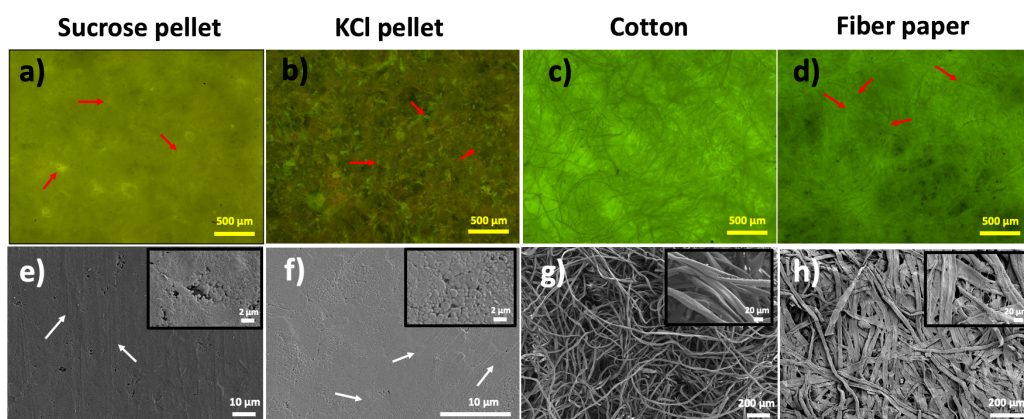


Figure 3. 7 a) Fluorescence microscopy, b) SEM images of sucrose pellet, KCl pellet, cotton, and fiber paper samples, including *P. harmala* extract. (Scale bars of fluorescence microscope images are 500 μm . Scale bars of SEM images are (e) and (f): 110 μm and (g) and (h): 200 μm . Scale bars of insets are (e) and (f): 2 μm and (g) and (h): 20 μm). Fluorescence microscope images were taken under an excitation wavelength of 450 nm.

Compared to the crystal-based monoliths, cellulose-based cotton and fiber paper revealed fibrillar structures in both fluorescence microscopy and SEM images (Figure 3.7c, d, g and h). In the fluorescence microscopy images, “fiber paper” fibers appeared more flattened compared to cotton fibers, as shown with red arrows in Figure 3.7d. To understand the structural details, we performed SEM imaging. As represented in Figure 3.7g and h, we observe a thicker and more flattened fiber structure in the paper in contrast to the cotton, which supports the images obtained by fluorescence microscope. Furthermore, SEM images indicated that cotton fibers have a diameter of $16.8 \pm 4.6 \mu\text{m}$ and appeared to have a more helical shape. On the other hand, in fiber paper, it seems like thinner fibers come together and form these thick fibers having a diameter of $28.9 \pm 8.6 \mu\text{m}$. Also, many short extensions between the fibers are visible in SEM images. For further structural investigation, we also performed Scanning Transmission Electron Microscopy (STEM) (Figure 3.8).

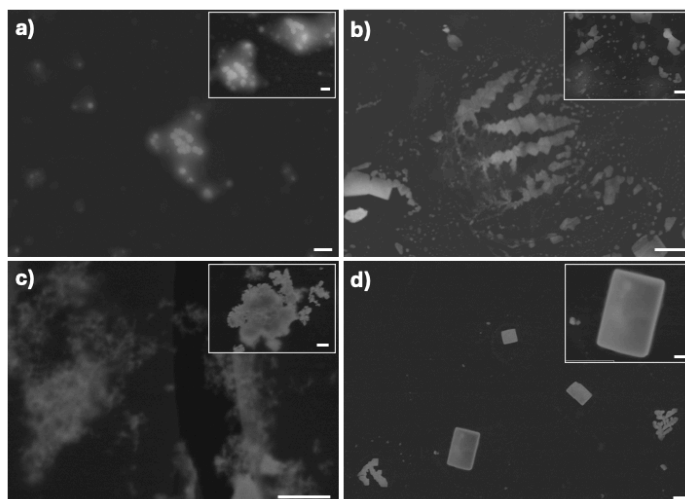


Figure 3. 8 a) STEM images of sucrose crystal powders including *Peganum harmala*, b) KCl crystal powders including *Peganum harmala*, c) sucrose crystal powders without *Peganum harmala* extract (sucrose control group), d) KCl crystal powders without *Peganum harmala* extract (KCl control group). Insets represent the magnified images of the respective groups. The scale bars indicate 2 μm for the main images and 1 μm for the insets.

STEM images of *P. harmala*, including sucrose crystal powders and KCl crystal powders, revealed that sucrose crystals predominantly displayed spherical structures, while salt crystals exhibited cube or rectangle shapes (Figure 3.8a-d). Notably, the localized structure of salt crystals depicted in Figure 3.3 was also confirmed through STEM imaging (Figure 3.8b and d). Our findings indicate that the sucrose crystal powders including *P. harmala* and KCl crystal powders including *P. harmala* have similar average sizes and standard deviations (Figure 3.8a, b and Table 3.2). While sucrose powder shapes and sizes are similar independent of the presence of *P. harmala*, adding *P. harmala* extract to KCl makes the shapes of the observed features more isotropic and reduces the feature size. We also would like to highlight that we did not observe any indication of the presence of a low-dimensional system that could significantly affect the emission features of the semiconducting molecules in the extract. However, it is worth noting that the electron beams accelerated under a high voltage in the STEM instrument causes melting in the organic molecules, which makes it very challenging to get high-resolution and high-magnification images.

Table 3. 2 The average sizes and standard deviations of the crystal powders calculated from STEM images using the Image J program.

Groups	Average Size	Standart Deviation
<i>Peganum harmala</i> in sucrose crystal powder	383 nm	142 nm
<i>Peganum harmala</i> in KCl crystal powder	345 nm	124 nm
Only sucrose crystal powder	324 nm	136 nm
Only KCl crystal powder	1.5 μm	1.8 μm

Subsequent to structural characterization, the fluorescence quantum yield (QY) and PL spectra of all *P. harmala* solid samples were measured and presented in Figure 3.9a. QY measurements revealed that the extract-embedded paper has the highest QY measured as 44.7%, decreased from 75.6% in the liquid state, which makes it suitable for a proof-of-concept LED application.

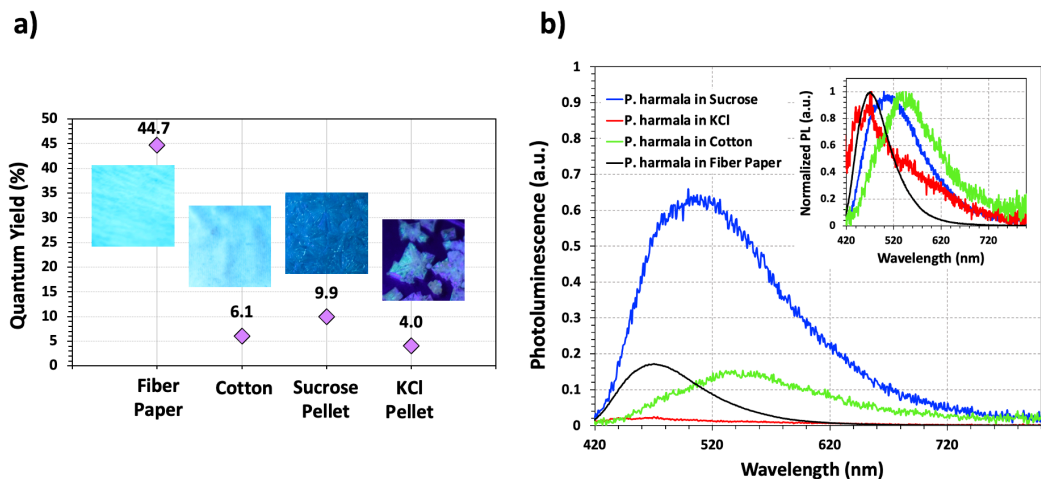


Figure 3. 9 a) Quantum yields of *P. harmala* incorporated hosts presented together with their photos under UV illumination, b) photoluminescence spectra of *P. harmala* extract within the solid matrices. Inset shows the photoluminescence spectra normalized according to peak values.

Interestingly, although cotton also has a fibrous structure, the QY of this sample remained at 6.1%. There could be two explanations for this decreased quantum efficiency. The first one is that cotton's absorption capacity of extracts is higher than that of the paper. As a

result, significantly more extracts are soaked by the cotton. This means that more fluorescent biomolecules are found between solid cotton fibers and are close to each other leading to the quenching of the QY. The other possible explanation for the decreased QY is the difference in fiber structures between cotton and fiber paper. In the paper, wide, flat, and interconnected fibers increasing the surface area (Figure 3.7h) might also increase the distribution of the biomolecules after embedding, which may have caused less aggregation than the cotton. However, cotton possesses helical and thinner fibers (Figure 3.7g), possibly leading to a more serious aggregation and, thus, quenching.

Then we analyzed the *P. harmala* fluorescence spectra within all matrices. As observed in Figure 3.9b, the maximum PL peaks were identified as 470 nm for *P. harmala* in fiber paper, 550 nm for *P. harmala* in cotton, 455 nm for *P. harmala* in KCl monoliths, and 509 nm for *P. harmala* in sucrose monoliths while the *P. harmala* extract is at 490 nm. When we specifically compare the fibrous matrices that have the highest QYs, we observe that the fiber paper (44.7% QY) has a blue shift (490 to 470 nm), while cotton (6.1% QY) has a very strong redshift (490 to 545 nm). We attribute this redshift observed in cotton to the nonradiative interaction between fluorophore molecules in close proximity due to high amount of fluorophores end up in cotton owing to its very high absorption capability. However, the blue-shift observed in fiber paper and a very high QY clearly suggest that this matrix passivates the nonradiative transitions in the extract. To evaluate the effect of the extract volume and the embedding time, we also embedded the paper in the extract for 30 min instead of 2 min and dropped the same volume (2 mL) onto the fiber paper slowly to allow the matrix to incorporate all of the extract solution. Results demonstrated that 30 minutes embedding and dropping techniques resulted in QYs of 37.6% and 34.6% as presented in Figure 3.10.

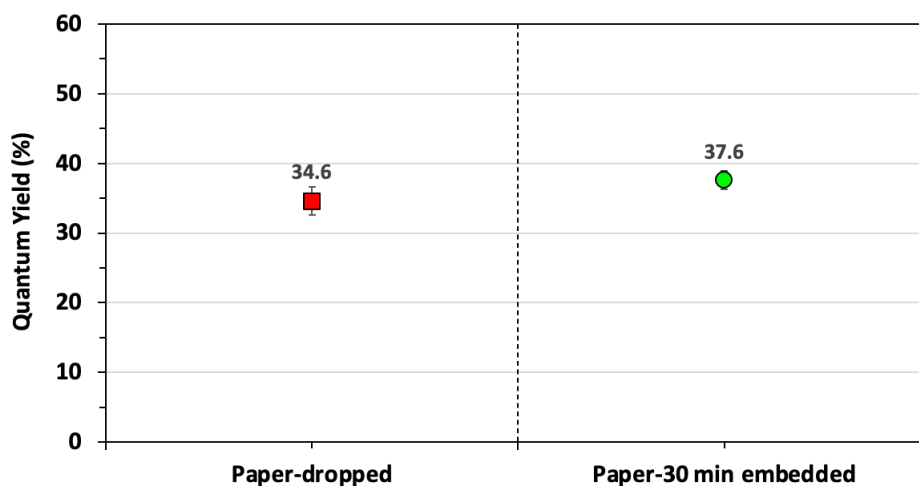


Figure 3. 10 Quantum yields of *P. harmala* dropped papers and 30 min embedded papers.

This result demonstrated that although there is a slight decrease from 46% to 34–37% with increasing embedding time or absorbed volume, we still have a very high QY compared to other groups having QYs lower than 10%. This result is interesting because cotton also has a fibrous structure; however, we do not see a similar increase in its QY. This suggests that the fiber paper's flat and highly interconnected structure might induce a more homogenous distribution within the matrix.

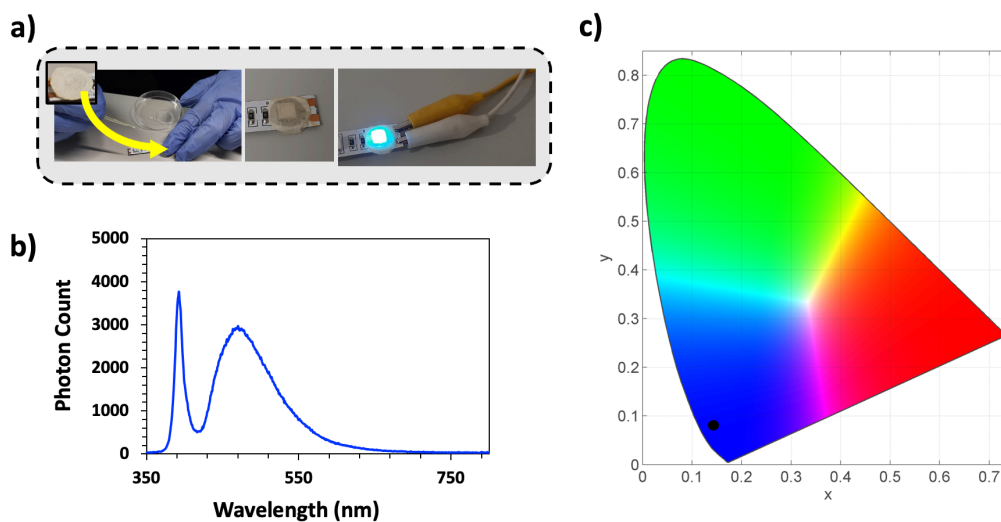


Figure 3. 11 (a) Representative image of the integration of the color-converting *P. harmala* embedded paper with the LED, (b) LED emission spectrum under 5 mA current flow, and (c) CIE 1931 color coordinates of the obtained LED on the chromaticity diagram.

Finally, we prepared a proof-of-concept LED employing the sustainable, bio-based color converters. Since we obtained the highest QY with the sample in the paper host, we used it as a biocompatible and easy-to-handle color converter on the LED chip emitting at ~ 400 nm. The representative image showing the fabrication of the LED setup is given in Figure 3.11a and the results are demonstrated in Figure 3.11b and c. The LED we designed exhibited a blueish emission as quantified by the CIE 1931 color coordinates (0.139, 0.070). Although the extract has a cyan-green emission, the LED chip exciting the color-converting material shifted the color towards a more blueish region. We measured the luminous efficiency of our device as $21.9 \text{ lm W}_{\text{elect}}^{-1}$, which is relatively close to the performance of commercial epitaxially grown LED chips, showing the potential of plant extracts as color converters for SSL.

Chapter 4

Conclusion and Future Prospects

4.1 Conclusion

This thesis explores sustainable, natural, and environmentally friendly innovative designs of two different plant extracts (*Hypericum perforatum* and *Peganum harmala*) for biomedical and optical applications.

In the first study, a medicinal plant known as *Hypericum perforatum* was utilized for the green synthesis of ZnO nanoparticles (ZnO NPs). Although many studies are reporting the wound-healing success of this plant [84], there are very limited reports related to its anti-cancer effect. As far as we know, this is the first study investigating both *Hypericum perforatum* extract and its green synthesized ZnO nanoparticles against liver cancer using Hep-G2 cell line. Another key novelty of this study lies in the ZnO NP synthesis process. In addition to commonly studied parameters such as pH and temperature, we systematically examined the effect of UV exposure during synthesis to assess its impact on the structural properties of the resulting ZnO NPs. The synthesized nanoparticles were then characterized using UV-Vis spectroscopy, X-ray diffraction (XRD), scanning electron microscopy (SEM) to determine their optical features, crystalline structure, morphology, and functional groups, respectively. In order to evaluate the biological activity of the bare *Hypericum perforatum* and two ZnO NPs having spherical and plate-like shape, we conducted cytotoxicity studies on Hep-G2, human liver cancer cell line, and antibacterial studies against both gram positive (*S. aureus*) and gram negative (*E. coli*) bacteria species. Our results demonstrated a dose-dependent inhibition of cell viability, with significant cytotoxic effects observed at higher concentrations, indicating the potential of ZnO NPs as a therapeutic agent for liver cancer treatment. However, there was no significant effect in terms of antibacterial activity. In the second study, we report

a natural, cost-effective, easy-to-handle paper-based color converter utilized from fluorescent *P. harmala* extract, which can be a promising alternative to its counterparts in solid-state lighting. In the literature, there are many studies reporting a significant quantum yield decrease of organic liquids [85] or inorganic [86] fluorophores with solid-state transition. A major challenge in the field is the significant decrease in quantum yield observed when liquid organic or inorganic fluorophores transition to the solid state, which limits their industrial applications. This issue is even more pronounced in plant-based fluorescent biomolecules due to two key drawbacks: (1) the difficulty of finding a plant extract with a high quantum yield and (2) the challenge of maintaining this high quantum efficiency in the solid state. To address these challenges, we investigated the high quantum yield transition of a natural and sustainable plant extract to inexpensive and easy-to-handle crystal-based and cellulose fiber-based solid matrices for solid-state lighting applications. As a crystal-based platform, we incorporated *P. harmala* extract into sucrose and KCl crystals. In parallel, we explored fiber-based hosts, including cotton pads and fiber paper, to investigate their potential as a solid scaffold. Structural characterizations demonstrated that, except for KCl crystals, the extract is relatively homogeneously distributed within the solid host matrices. However, QY measurements revealed that the highest quantum efficiency is observed in fiber paper as 44.7%, thanks to its structural advantages. In contrast, QYs of the other matrices become less than 10%. As a proof-of-concept demonstration, we presented the use of *P. harmala* extract-embedded fiber paper as a color converter on an LED. The obtained device possessed a blue emission and exhibited a luminous efficiency of $21.9 \text{ lm W}_{\text{elect}}^{-1}$ showing that *Peganum harmala* extract incorporating solids are excellent candidates as color converters. We believe these findings pave the way for the broader adoption of plant-based materials in sustainable lighting technologies.

4.2 Societal Impact and Contribution to Global

This research contributes to sustainable scientific advancements in both healthcare and technology by utilizing plant-based materials to develop environmentally friendly solutions.

The first part of the study demonstrated the anticancer activity of green-synthesized ZnO nanoparticles against Hep-G2 liver cancer cells, offering a cost-effective and sustainable alternative to conventional treatments. These nanoparticles were synthesized using

Hypericum perforatum instead of chemical methods, ensuring the use of non-toxic and readily available materials. This approach not only reduces environmental impact but also makes cancer treatment more accessible, particularly in resource-limited settings. These findings align with the United Nations Sustainable Development Goals (SDGs), particularly Good Health and Well-being (SDG 3) and Responsible Consumption and Production (SDG 12).

The second part of the study focused on developing a paper-based color converter for LED systems using fluorescent *Peganum harmala* extract. Our results indicate that this bio-based converter serves as an environmentally friendly and cost-effective alternative to current commercial solutions. Additionally, its excellent optical properties make it a promising candidate for next generation display technologies and lighting systems enhancing both sustainability and visual performance. Since plant-based color converters are biodegradable, they simplify disposal and recycling in lighting devices, further contributing to Affordable and Clean Energy (SDG 7) by promoting energy-efficient solutions.

Overall, this research demonstrates the potential of plant-based materials in advancing both healthcare and lighting technologies. The ZnO nanoparticles synthesized from *Hypericum perforatum* offer a promising direction for cancer research, while the biomolecule-derived color converter from *Peganum harmala* presents a sustainable innovation for solid-state lighting systems.

4.3 Future Prospects

Plant-based biomaterials hold significant potential for future research and industrial applications, offering sustainable and eco-friendly alternatives across multiple fields.

The green-synthesized zinc oxide nanoparticles developed in this study pave the way for biocompatible and environmentally friendly nanomedicines. With further optimization, these nanoparticles could be employed in targeted cancer therapies, improving treatment efficacy while minimizing toxicity. Additionally, scaling up their synthesis for industrial production could expand their applications beyond healthcare, making them promising candidates for personal care products and pharmaceuticals.

Similarly, the color converter based on biomolecules from *Peganum harmala* presents exciting opportunities for advancing solid-state lighting systems. By improving their optical properties and stability, these bio-based converters can contribute to the

development of energy-efficient and sustainable lighting technologies. Considering the toxicity and sustainability concerns associated with quantum-dot-based color converters, these eco-friendly sustainable color converters have strong potential for industrial adoption as safer and more sustainable replacements for conventional materials.

In conclusion, future studies on fluorescent plant-based materials can drive innovation in nanomedicine, renewable energy, and sustainable manufacturing. Moreover, the optimization of these materials for enhanced performance, stability, and scalability can play a transformative role in both scientific and industrial advancements.



BIBLIOGRAPHY

- [1] “Indian Journal of Pharmacology.” Accessed: Dec. 03, 2024. [Online]. Available: https://journals.lww.com/iphr/citation/2000/32040/pharmacology_of_medicinal_plants_and_natural.11.aspx
- [2] C. SS, N. M, K. E, and E. C, “Antidepressant activity of hypericum perforatum and hyperforin: the neglected possibility,” *Pharmacopsychiatry*, vol. 31 Suppl 1, no. SUPPL. 1, pp. 7–15, 1998, doi: 10.1055/S-2007-979340.
- [3] “The Biological Activities of Hypericum perforatum L. | ISPEC Journal of Agricultural Sciences.” Accessed: Dec. 04, 2024. [Online]. Available: <https://ispecjournal.com/index.php/ispecjas/article/view/622>
- [4] K. M. Klemow, A. Bartlow, J. Crawford, N. Kocher, J. Shah, and M. Ritsick, “Medical Attributes of St. John’s Wort (Hypericum perforatum),” *Herbal Medicine: Biomolecular and Clinical Aspects: Second Edition*, pp. 211–237, Mar. 2011, doi: 10.1201/b10787-12.
- [5] A. Rostami and M. Rabiee, “Anthocyanins extract as a non-toxic and green fluorescent label for bioimaging of HER2-positive breast cancer cells,” *Environ Res*, vol. 237, no. Pt 2, Nov. 2023, doi: 10.1016/J.ENVRES.2023.116878.
- [6] O. Erdogan *et al.*, “Green synthesis of silver nanoparticles via Cynara scolymus leaf extracts: The characterization, anticancer potential with photodynamic therapy in MCF7 cells,” *PLoS One*, vol. 14, no. 6, p. e0216496, Jun. 2019, doi: 10.1371/JOURNAL.PONE.0216496.
- [7] D. Suhag, P. Thakur, and A. Thakur, “Introduction to nanotechnology,” *Integrated Nanomaterials and their Applications*, pp. 1–17, Dec. 2023, doi: 10.1007/978-981-99-6105-4_1.
- [8] C. Buzea, I. I. Pacheco, and K. Robbie, “Nanomaterials and nanoparticles: sources and toxicity,” *Biointerphases*, vol. 2, no. 4, pp. MR17–MR71, Dec. 2007, doi: 10.1116/1.2815690.
- [9] S. Parveen, R. Misra, and S. K. Sahoo, “Nanoparticles: a boon to drug delivery, therapeutics, diagnostics and imaging,” *Nanomedicine*, vol. 8, no. 2, pp. 147–166, Feb. 2012, doi: 10.1016/J.NANO.2011.05.016.
- [10] R. Singh and J. W. Lillard, “Nanoparticle-based targeted drug delivery,” *Exp Mol Pathol*, vol. 86, no. 3, pp. 215–223, Jun. 2009, doi: 10.1016/J.YEXMP.2008.12.004.
- [11] S. Sim and N. K. Wong, “Nanotechnology and its use in imaging and drug delivery (Review),” *Biomed Rep*, vol. 14, no. 5, p. 42, 2021, doi: 10.3892/BR.2021.1418.
- [12] K. K. Jain, “Nanotechnology in clinical laboratory diagnostics,” 2005. doi: 10.1016/j.cccn.2005.03.014.
- [13] M. E. A. El-Hack *et al.*, “Nutritional and pharmaceutical applications of nanotechnology: Trends and advances,” 2017. doi: 10.3923/ijp.2017.340.350.
- [14] F. Li *et al.*, “Effect of Ball Milling Parameters on Properties of Nano-Sized Tungsten Powder via Mechanochemical Processing,” *Metals (Basel)*, vol. 14, no. 9, p. 1079, Sep. 2024, doi: 10.3390/MET14091079/S1.
- [15] M. Kim, S. Osone, T. Kim, H. Higashi, and T. Seto, “Synthesis of Nanoparticles by Laser Ablation: A Review,” *KONA Powder and Particle Journal*, vol. 34, no. 34, pp. 80–90, 2017, doi: 10.14356/KONA.2017009.
- [16] D. M. Mattox, *Handbook of Physical Vapor Deposition (PVD) Processing*. Elsevier Inc., 2010. Accessed: Dec. 08, 2024. [Online]. Available: <http://www.sciencedirect.com:5070/book/9780815520375/handbook-of-physical-vapor-deposition-pvd-processing>

- [17] H. D. Beyene, A. A. Werkneh, H. K. Bezabh, and T. G. Ambaye, "Synthesis paradigm and applications of silver nanoparticles (AgNPs), a review," *Sustainable Materials and Technologies*, vol. 13, pp. 18–23, Sep. 2017, doi: 10.1016/J.SUSMAT.2017.08.001.
- [18] C. J. Brinker and G. W. Scherer, "Sol-Gel Science: The Physics and Chemistry of Sol-Gel Processing," *Sol-Gel Science: The Physics and Chemistry of Sol-Gel Processing*, pp. 1–908, Oct. 2013, doi: 10.1016/C2009-0-22386-5.
- [19] I. Capek, "Preparation of metal nanoparticles in water-in-oil (w/o) microemulsions," 2004. doi: 10.1016/j.cis.2004.02.003.
- [20] P. Singh, Y. J. Kim, D. Zhang, and D. C. Yang, "Biological Synthesis of Nanoparticles from Plants and Microorganisms," 2016. doi: 10.1016/j.tibtech.2016.02.006.
- [21] M. Zakir *et al.*, "The green synthesis of biocompatible nanocomposites and its application for the on-target delivery of the anticancer drugs," *J Mater Res*, vol. 39, no. 3, pp. 325–341, Feb. 2024, doi: 10.1557/S43578-023-01208-1/FIGURES/10.
- [22] S. A. Saiqa Ikram, "Silver Nanoparticles: One Pot Green Synthesis Using Terminalia arjuna Extract for Biological Application," *J Nanomed Nanotechnol*, vol. 06, no. 04, 2015, doi: 10.4172/2157-7439.1000309.
- [23] A. K. Mittal, Y. Chisti, and U. C. Banerjee, "Synthesis of metallic nanoparticles using plant extracts," 2013. doi: 10.1016/j.biotechadv.2013.01.003.
- [24] S. Irvani, "Green synthesis of metal nanoparticles using plants," *Green Chemistry*, vol. 13, no. 10, 2011, doi: 10.1039/c1gc15386b.
- [25] J. Kim *et al.*, "Green synthesis of multi-functional silver and gold nanoparticles from the oriental herbal adaptogen: Siberian ginseng aglycone ginsenoside-polyethylene glycol conjugates: synthesis, physicochemical characterizations, and in vitro studies," *Artif Cells Nanomed Biotechnol Artif Cells Nanomed Biotechnol Int J Nanomedicine Int J Syst Evol Microbiol. Arch Microbiol Apr Ramya Mathiyalagan, Yeon-. Artif Cells Nanomed Biotechnol Artif Cells Nanomed Biotechnol International Journal*, vol. 44, no. 447, 2016.
- [26] A. H. Al Sharie *et al.*, "Green synthesis of zinc oxide nanoflowers using Hypericum triquetrifolium extract: characterization, antibacterial activity and cytotoxicity against lung cancer A549 cells," *Appl Organomet Chem*, vol. 34, no. 8, 2020, doi: 10.1002/aoc.5667.
- [27] Ü. Özgür *et al.*, "A comprehensive review of ZnO materials and devices," 2005. doi: 10.1063/1.1992666.
- [28] S. J. Pearton, D. P. Norton, K. Ip, Y. W. Heo, and T. Steiner, "Recent progress in processing and properties of ZnO," 2005. doi: 10.1016/j.pmatsci.2004.04.001.
- [29] S. Baruah and J. Dutta, "Hydrothermal growth of ZnO nanostructures," *Sci Technol Adv Mater*, vol. 10, no. 1, 2009, doi: 10.1088/1468-6996/10/1/013001.
- [30] F. S. and Dr. S. R. Brintha, "Synthesis And Characterization Of ZnO-Cdo Nanocomposite And Its Antibacterial Activity," *J Pharm Negat Results*, 2022.
- [31] Z. L. Wang, "Zinc oxide nanostructures: Growth, properties and applications," *Journal of Physics Condensed Matter*, vol. 16, no. 25, 2004, doi: 10.1088/0953-8984/16/25/R01.
- [32] N. Jones, B. Ray, K. T. Ranjit, and A. C. Manna, "Antibacterial activity of ZnO nanoparticle suspensions on a broad spectrum of microorganisms," *FEMS Microbiol Lett*, vol. 279, no. 1, 2008, doi: 10.1111/j.1574-6968.2007.01012.x.

- [33] V. Butterweck and M. Schmidt, "St. John's wort: Role of active compounds for its mechanism of action and efficacy," *Wiener Medizinische Wochenschrift*, vol. 157, no. 13–14, 2007, doi: 10.1007/s10354-007-0440-8.
- [34] V. Butterweck, G. Jürgenliemk, A. Nahrstedt, and H. Winterhoff, "Flavonoids from *Hypericum perforatum* show antidepressant activity in the forced swimming test," *Planta Med*, vol. 66, no. 1, pp. 3–6, 2000, doi: 10.1055/S-2000-11119/ID/5/BIB.
- [35] B. Farasati Far *et al.*, "The potential role of *Hypericum perforatum* in wound healing: A literature review on the phytochemicals, pharmacological approaches, and mechanistic perspectives," *Phytotherapy Research*, vol. 38, no. 7, pp. 3271–3295, Jul. 2024, doi: 10.1002/PTR.8204.
- [36] D. D. Ciccarelli, A. Cesare Andreucci, and A. M. Pagni, "The 'black nodules' of *hypericum perforatum* l. subsp. *perforatum*: Morphological, anatomical, and histochemical studies during the course of ontogenesis," *Isr J Plant Sci*, vol. 49, no. 1, pp. 33–40, 2001, doi: 10.1560/46Y5-AFWD-TCY0-KGFG.
- [37] N. Öztrk, M. Tunçel, and S. Potoğlu-Erkara, "Phenolic compounds and antioxidant activities of some *Hypericum* species: A comparative study with *H. perforatum*," *Pharm Biol*, vol. 47, no. 2, pp. 120–127, Feb. 2009, doi: 10.1080/13880200802437073.
- [38] R. Tsao, "Chemistry and biochemistry of dietary polyphenols," 2010. doi: 10.3390/nu2121231.
- [39] I. Hussain, N. B. Singh, A. Singh, H. Singh, and S. C. Singh, "Green synthesis of nanoparticles and its potential application," 2016. doi: 10.1007/s10529-015-2026-7.
- [40] X. Zhao *et al.*, "(±)-Hyperpyran A: Terpenoid-based bicyclic dihydropyran enantiomers with hypoglycemic activity from *Hypericum perforatum* (St. John's wort)," *Fitoterapia*, vol. 161, p. 105221, Sep. 2022, doi: 10.1016/J.FITOTE.2022.105221.
- [41] N. Bala *et al.*, "Green synthesis of zinc oxide nanoparticles using *Hibiscus subdariffa* leaf extract: effect of temperature on synthesis, anti-bacterial activity and anti-diabetic activity," *RSC Adv*, vol. 5, no. 7, pp. 4993–5003, Dec. 2014, doi: 10.1039/C4RA12784F.
- [42] J. Xu, Y. Huang, S. Zhu, N. Abbes, X. Jing, and L. Zhang, "A review of the green synthesis of ZnO nanoparticles using plant extracts and their prospects for application in antibacterial textiles," *J Eng Fiber Fabr*, vol. 16, Sep. 2021, doi: 10.1177/15589250211046242/ASSET/IMAGES/LARGE/10.1177_15589250211046242-FIG6.JPEG.
- [43] M. E. Cervantes-Gaxiola, F. A. Vázquez-González, E. Y. Rios-Irbe, P. F. Méndez-Herrera, and C. Leyva, "Effect of pH on the green synthesis of ZnO nanoparticles using *Sorghum bicolor* seed extract and their application in photocatalytic dye degradation," *Mater Lett*, vol. 372, p. 136982, Oct. 2024, doi: 10.1016/J.MATLET.2024.136982.
- [44] D. Skalkos, E. Gioti, C. D. Stalikas, H. Meyer, T. G. Papazoglou, and G. Filippidis, "Photophysical properties of *Hypericum perforatum* L. extracts – Novel photosensitizers for PDT," *J Photochem Photobiol B*, vol. 82, no. 2, pp. 146–151, Feb. 2006, doi: 10.1016/J.JPHOTOBIO.2005.11.001.
- [45] H. R. Madan *et al.*, "Facile green fabrication of nanostructure ZnO plates, bullets, flower, prismatic tip, closed pine cone: Their antibacterial, antioxidant, photoluminescent and photocatalytic properties," *Spectrochim Acta A Mol Biomol Spectrosc*, vol. 152, pp. 404–416, Jan. 2016, doi: 10.1016/J.SAA.2015.07.067.

- [46] M. Ramesh, M. Anbuvaran, and G. Viruthagiri, "Green synthesis of ZnO nanoparticles using Solanum nigrum leaf extract and their antibacterial activity," *Spectrochim Acta A Mol Biomol Spectrosc*, vol. 136, no. PB, pp. 864–870, Feb. 2015, doi: 10.1016/J.SAA.2014.09.105.
- [47] S. M. Mahdi Ismail, S. M. Ahmed, A. F. Abdulrahman, and M. A. AlMessiere, "Characterization of green synthesized ZnO nanoparticles by using pinus brutia leaves extracts," *J Mol Struct*, vol. 1280, p. 135063, May 2023, doi: 10.1016/J.MOLSTRUC.2023.135063.
- [48] S. Shaziman, A. S. Ismailrosdi, M. H. Mamat, and A. S. Zoolfakar, "Influence of Growth Time and Temperature on the Morphology of ZnO Nanorods via Hydrothermal," *IOP Conf Ser Mater Sci Eng*, vol. 99, no. 1, p. 012016, Nov. 2015, doi: 10.1088/1757-899X/99/1/012016.
- [49] E. F. Schubert, "Light-emitting diodes, second edition," *Light-emitting Diodes, Second Edition*, vol. 9780521865388, pp. 1–422, Jan. 2006, doi: 10.1017/CBO9780511790546.
- [50] S. O. Kasap, "Optoelectronics and Photonics: Principles and Practices (2nd Edition) Chapter 1," *Optoelectronics and Photonics: Principles and Practices (2nd Edition) Chapter 1*, p. Chapter 4, 2012, Accessed: Nov. 29, 2024. [Online]. Available: https://books.google.com/books/about/Optoelectronics_and_Photonics.html?hl=tr&id=P248MAEACAAJ
- [51] Y. Zhang, L. Luo, G. Chen, Y. Liu, R. Liu, and X. Chen, "Green and red phosphor for LED backlight in wide color gamut LCD," *Journal of Rare Earths*, vol. 38, no. 1, pp. 1–12, Jan. 2020, doi: 10.1016/J.JRE.2019.10.005.
- [52] "Graydon: The new oil - Google Scholar." Accessed: Nov. 29, 2024. [Online]. Available: <https://scholar.google.com/scholar?cluster=11565791805648709626&hl=en&oi=scholar>
- [53] T. Erdem and H. V. Demir, "Color science of nanocrystal quantum dots for lighting and displays," *Nanophotonics*, vol. 2, no. 1, pp. 57–81, Feb. 2013, doi: 10.1515/NANOPH-2012-0031/ASSET/GRAPHIC/NANOPH-2012-0031_FIG27.JPG.
- [54] B. Gidwani *et al.*, "Quantum dots: Prospectives, toxicity, advances and applications," *J Drug Deliv Sci Technol*, vol. 61, p. 102308, Feb. 2021, doi: 10.1016/J.JDDST.2020.102308.
- [55] "High-Stability, High-Efficiency Organic Monoliths Made of Oligomer Nanoparticles Wrapped in Organic Matrix | Enhanced Reader."
- [56] R. Duval and C. Duplais, "Correction: Fluorescent natural products as probes and tracers in biology," *Nat Prod Rep*, vol. 34, no. 3, pp. 329–329, Mar. 2017, doi: 10.1039/C7NP90008B.
- [57] W. H. Talib, I. Alsalahat, S. Daoud, R. F. Abutayeh, and A. I. Mahmud, "Plant-Derived Natural Products in Cancer Research: Extraction, Mechanism of Action, and Drug Formulation," *Molecules*, vol. 25, no. 22, Nov. 2020, doi: 10.3390/MOLECULES25225319.
- [58] A. Kumar, S. Aswal, R. B. Semwal, A. Chauhan, S. K. Joshi, and D. K. Semwal, "Role of plant-derived alkaloids against diabetes and diabetes-related complications: a mechanism-based approach," *Phytochemistry Reviews*, vol. 18, no. 5, pp. 1277–1298, Oct. 2019, doi: 10.1007/S11101-019-09648-6.
- [59] M. Moloudizargari, P. Mikaili, S. Aghajanshakeri, M. Asghari, and J. Shayegh, "Pharmacological and therapeutic effects of Peganum harmala and its main

- alkaloids,” *Pharmacogn Rev*, vol. 7, no. 14, pp. 199–212, Jul. 2013, doi: 10.4103/0973-7847.120524.
- [60] L. Donaldson, “Autofluorescence in Plants,” *Molecules* 2020, Vol. 25, Page 2393, vol. 25, no. 10, p. 2393, May 2020, doi: 10.3390/MOLECULES25102393.
- [61] L. Donaldson, “Autofluorescence in plants,” *Molecules*, vol. 25, no. 10, May 2020, doi: 10.3390/MOLECULES25102393.
- [62] P. Singh, Y. J. Kim, D. Zhang, and D. C. Yang, “Biological Synthesis of Nanoparticles from Plants and Microorganisms,” *Trends Biotechnol*, vol. 34, no. 7, pp. 588–599, Jul. 2016, doi: 10.1016/J.TIBTECH.2016.02.006.
- [63] L. Wang, Z. Lou, K. Jiang, and G. Shen, “Bio-Multifunctional Smart Wearable Sensors for Medical Devices,” *Advanced Intelligent Systems*, vol. 1, no. 5, Sep. 2019, doi: 10.1002/AISY.201900040.
- [64] N. T. Mary Rosana, D. Joshua Amarnath, P. Senthil Kumar, and K. L. Vincent Joseph, “Potential of plant-based photosensitizers in dye-sensitized solar cell applications,” *Environ Prog Sustain Energy*, vol. 39, no. 3, p. e13351, May 2020, doi: 10.1002/EP.13351.
- [65] Z. Bi *et al.*, “Biomass-derived porous carbon materials with different dimensions for supercapacitor electrodes: a review,” *J Mater Chem A Mater*, vol. 7, no. 27, pp. 16028–16045, Jul. 2019, doi: 10.1039/C9TA04436A.
- [66] P. Roy *et al.*, “Plant leaf-derived graphene quantum dots and applications for white LEDs,” *New Journal of Chemistry*, vol. 38, no. 10, pp. 4946–4951, Sep. 2014, doi: 10.1039/C4NJ01185F.
- [67] V. Singh and A. K. Mishra, “White Light Emission from Vegetable Extracts,” *Scientific Reports* 2015 5:1, vol. 5, no. 1, pp. 1–9, Jun. 2015, doi: 10.1038/srep11118.
- [68] “An in vitro evaluation of human DNA topoisomerase I inhibition by Peganum harmala L. seeds extract and its beta-carboline alkaloids - PubMed.” Accessed: Nov. 29, 2024. [Online]. Available: <https://pubmed.ncbi.nlm.nih.gov/12042115/>
- [69] F. Fathiazad, Y. Azarmi, and L. Khodaie, “Pharmacological Effects of Peganum harmala Seeds Extract on Isolated Rat Uterus: Effects of Peganum harmala on rat uterus,” *Iranian Journal of Pharmaceutical Sciences*, vol. 2, no. 2, pp. 81–86, Apr. 2006, doi: 10.22037/IJPS.V2.39553.
- [70] G. H. Chang, W. J. Wang, Z. X. Yin, B. Yue, J. X. Wang, and T. P. Gao, “Changes on available phosphorus and total nitrogen contents from soil around roots of two desert plants,” *E3S Web of Conferences*, vol. 293, Jul. 2021, doi: 10.1051/E3SCONF/202129301002.
- [71] “Asgarpanah, J. and Ramezanloo Chemistry, F. (2012) Chemistry, Pharmacology and Medicinal Properties of Peganum harmala L. African Journal of Pharmacy and Pharmacology, 6, 1573-1580. - References - Scientific Research Publishing.” Accessed: Nov. 29, 2024. [Online]. Available: <https://www.scirp.org/reference/referencespapers?referenceid=1617953>
- [72] “Antibacterial activity of different parts of Peganum harmala L. growing in Iran against multi-drug resistant bacteria - PubMed.” Accessed: Nov. 29, 2024. [Online]. Available: <https://pubmed.ncbi.nlm.nih.gov/29033706/>
- [73] L. Lewerenz, T. Hijazin, S. Abouzeid, R. Hänsch, and D. Selmar, “Pilot study on the uptake and modification of harmaline in acceptor plants: An innovative approach to visualize the interspecific transfer of natural products,” *Phytochemistry*, vol. 174, p. 112362, Jun. 2020, doi: 10.1016/J.PHYTOCHEM.2020.112362.

- [74] S. A. Fahmy, I. M. Fawzy, B. M. Saleh, M. Y. Issa, U. Bakowsky, and H. M. E. S. Azzazy, "Green synthesis of platinum and palladium nanoparticles using Peganum harmala L. Seed alkaloids: Biological and computational studies," *Nanomaterials*, vol. 11, no. 4, p. 965, Apr. 2021, doi: 10.3390/NANO11040965/S1.
- [75] M. Azizi, S. Sedaghat, K. Tahvildari, P. Derakhshi, and A. Ghaemi, "Synthesis of silver nanoparticles using Peganum harmala extract as a green route," *Green Chem Lett Rev*, vol. 10, no. 4, pp. 420–427, Oct. 2017, doi: 10.1080/17518253.2017.1395081.
- [76] "Therapeutic potential of harmaline, a novel alkaloid, against cervical cancer cells in vitro: Apoptotic induction and DNA interaction study," *J Appl Biol Biotechnol*, pp. 1–8, 2018, doi: 10.7324/JABB.2018.60401.
- [77] B. Hemmateenejad, M. Shamsipur, F. Samari, T. Khayamian, M. Ebrahimi, and Z. Rezaei, "Combined fluorescence spectroscopy and molecular modeling studies on the interaction between harmalol and human serum albumin," *J Pharm Biomed Anal*, vol. 67–68, pp. 201–208, Aug. 2012, doi: 10.1016/J.JPBA.2012.04.012.
- [78] T. Erdem, Z. Soran-Erdem, Y. Kelestemur, N. Gaponik, and H. V. Demir, "Excitonic improvement of colloidal nanocrystals in salt powder matrix for quality lighting and color enrichment," *Opt Express*, vol. 24, no. 2, p. A74, Jan. 2016, doi: 10.1364/OE.24.000A74.
- [79] Z. Soran-Erdem, T. Erdem, P. L. Hernandez-Martinez, M. Z. Akgul, N. Gaponik, and H. V. Demir, "Macrocrystals of colloidal quantum dots in anthracene: Exciton transfer and polarized emission," *Journal of Physical Chemistry Letters*, vol. 6, no. 9, pp. 1767–1772, May 2015, doi: 10.1021/ACS.JPCLETT.5B00685/SUPPL_FILE/JZ5B00685_SI_001.PDF.
- [80] Z. Soran-Erdem, T. Erdem, K. Gungor, J. Pennakalathil, D. Tuncel, and H. V. Demir, "High-Stability, High-Efficiency Organic Monoliths Made of Oligomer Nanoparticles Wrapped in Organic Matrix," *ACS Nano*, vol. 10, no. 5, pp. 5333–5339, May 2016, doi: 10.1021/ACSNANO.6B01473/ASSET/IMAGES/LARGE/NN-2016-01473Z_0007.JPEG.
- [81] X. Bai, F. Purcell-Milton, and Y. K. Gun'ko, "Macromatrices for nanoscale particles," *J Mater Chem C Mater*, vol. 10, no. 31, pp. 11105–11118, Aug. 2022, doi: 10.1039/D2TC01244H.
- [82] J. Hidalgo, E. Roldan, D. González-Arjona, M. Sánchez, A. Pardo, and J. M. L. Poyato, "Fluorescence lifetimes of some Harmala and Rauwolfia alkaloids," *J Photochem Photobiol A Chem*, vol. 41, no. 1, pp. 103–110, Feb. 1987, doi: 10.1016/1010-6030(87)80011-4.
- [83] H. T. Phuong, N. K. Thoa, P. T. A. Tuyet, Q. N. Van, and Y. D. Hai, "Cellulose Nanomaterials as a Future, Sustainable and Renewable Material," *Crystals 2022, Vol. 12, Page 106*, vol. 12, no. 1, p. 106, Jan. 2022, doi: 10.3390/CRYST12010106.
- [84] Damlar, O. F. Arpağ, U. Tatli, and A. Altan, "Effects of Hypericum perforatum on the healing of xenografts: a histomorphometric study in rabbits," *British Journal of Oral and Maxillofacial Surgery*, vol. 55, no. 4, pp. 383–387, May 2017, doi: 10.1016/J.BJOMS.2016.12.003.
- [85] A. Bergh, G. Craford, A. Duggal, and R. Haitz, "The Promise and Challenge of Solid-State Lighting," *Phys Today*, vol. 54, no. 12, pp. 42–47, Dec. 2001, doi: 10.1063/1.1445547.
- [86] S.-H. Chiu *et al.*, "Efficient hybrid white light-emitting diodes by organic-inorganic materials at different CCT from 3000K to 9000K," *Optics Express*, Vol.

23, *Issue 7*, pp. A204–A210, vol. 23, no. 7, pp. A204–A210, Apr. 2015, doi: 10.1364/OE.23.00A204.



CURRICULUM VITAE

2017 – 2022 B.Sc., Molecular Biology and Genetics, Abdullah Gül University,
Kayseri, TURKEY

2022 – Present M.Sc., Biongeneering, Abdullah Gül University,
Kayseri, TURKEY

SELECTED PUBLICATIONS

J1 Savas, M., Bozkurt, B., Akcan, D., Phul, R., vd. (2024). Semiconducting Plant Extracts of Cucurbita Pepo L. Seeds for Facile, Inexpensive, Fully Solution-Processed, Transparent Photodetector Fabrication. Erciyes Üniversitesi Fen Bilimleri Enstitüsü Fen Bilimleri Dergisi, 40(2), 372-382.

J2 Erdem, T., Orenc, A., Akcan, D., Duman, F., & Soran-Erdem, Z. (2024). Sustainable next-generation color converters from Peganum harmala seed extracts for solid-state lighting. RSC Advances, 14, 18528-1853.