CHAPTER 15

Nanotechnology and Medicinal Plant Extracts: A One Health Approach to Antibacterial Therapeutics

MUHAMMAD FURQAN[2], QURAT UL AIN ALAM[1], SEHAR JAVAD[1], AYESHA TANVEER[1], MUHAMMAD USMAN BARI[1], MARIA SOHAIL[3], ANEELA GUL[1*], BILAL ASLAM[1*]

[1]Institute of Physiology and Pharmacology, University of Agriculture, Faisalabad, Pakistan.
[2]College of Veterinary Sciences, FAHVS, The University of Agriculture, Peshawar, Pakistan.
[3]Department of Epidemiology & Public Health, University of Agriculture, Faisalabad, Pakistan.
*Corresponding author: aneelaguldvm14@gmail.com (A.G.), cba933@gmail.com (B.A.)

SUMMARY

"Nanotechnology and Medicinal Plant Extracts: A Health Approach to Antibacterial Therapy" examines in detail the relationship between these two technologies and their potential for antibacterial therapeutics. This approach combines nanotechnology concepts with the therapeutic properties of plants to address the growing problems of antibiotic resistance and the need for new potent antibiotics. Nanotechnology has the potential to revolutionize matter at the nanoscale, offering unique opportunities for drug delivery, enhanced antimicrobial activity, and targeted therapeutics By integrating chemical synthesis of plant material into nanoscale chemistry on the subject, researchers aim to exploit the inherent antimicrobial and targeted properties of these plants where pathogen transmission through controlled administration can provide the effectiveness has increased. The concept of a "one health" approach emphasizes how environmental, animal, and human health, are all interconnected. When this approach is applied to antimicrobial therapy, it is also important to consider the potential environmental impact and the effect of antibiotic resistance on humans and animals The combination of nanotechnology and extracts from medicinal plants enables the development of novel antibiotics that can overcome antibiotic resistance and reduce the side effects of conventional antibiotics using it to bring about it Further research, a collaboration of scientists, physicians and environmentalists is needed.

INTRODUCTION

The idea of "One Health" acknowledges the interdependence of environmental, animal, and human health and aims to advance multidisciplinary, cooperative methods of addressing problems with health that impact all three domains. (Buregyeya et al., 2021). It acknowledges that human, animal, and environmental health are intimately related and interrelated and that these relationships must be taken into consideration when addressing health issues. (Zinsstag et al., 2011). One Health approach may involve collaborations between public health professionals, veterinarians, ecologists, and other experts to identify and address health threats and promote health and well-being across all domains (de Garine-Wichatitsky et al., 2021). Antibacterial therapeutics refers to the use of medications, such as antibiotics, to treat bacterial infections (Marquet et al., 2015). Antibiotics work by targeting specific mechanisms or structures within bacterial cells (McCarter, 2017), which can either kill the bacteria or prevent them from multiplying (Begum et al., 2021). Antibacterial therapy can be used to treat meningitis, skin infections, pneumonia, urinary tract infections, and other bacterial disorders (Nauclér et al., 2021). It's important to keep in mind that antibiotics are only effective against bacterial infections; they are ineffective against viral illnesses like the flu or the common cold. The development of antibiotic-resistant bacteria as a result of inappropriate or overuse of antibiotics is one of the worst hazards to public health. Therefore, antibiotics should only be taken as directed by a healthcare provider and when prescribed (Prestinaci et al., 2015; Subramaniam & Girish, 2020).

The single health concept is increasingly being recognized as an important paradigm for addressing the global issue of

How to Cite: Furqan M, QuA Alam, S Javad, A Tanveer, MU Bari, M Sohail, A Gul & B Aslam, 2023. Nanotechnology and medicinal plant extracts: A One Health Approach to Antibacterial Therapeutics. In: Complementary and Alternative Medicine: One Health Perspective (Sindhu ZuD, B Aslam, U Uslu & M Mohsin, eds): FahumSci, Lahore, Pakistan, pp: 109-119. ISBN: 978-627-7745-01-1. https://doi.org/10.61748/CAM.2023/015

antimicrobial resistance, which poses serious threats to public health and affects human and animal welfare (Destoumieux-Garzón et al., 2018). Antimicrobial therapy is important in the fight against resistant infections, but issues such as inadequate or overuse of antibiotics methods like infection prevention poor management, and increasing bacterial resistance to antibiotics will hamper its effectiveness (Dugassa & Shukuri, 2017).

According to the One Health concept, antibiotic control efforts should take a comprehensive, multidisciplinary approach that addresses the interactions between environmental, animal, and human health around (Bonilla-Aldana et al., 2020). The one health perspective can help increase the effectiveness and sustainability of antibiotics by integrating socioeconomic considerations, environmental health, and human and animal health into efforts created to combat bacterial resistance(Collignon & McEwen, 2019). For example, a healthcare approach could promote the responsible use of antibiotics in veterinary and human medicine, for infection prevention and control strategies in clinical settings have increased, support sustainable agricultural practices to reduce the need for antibiotics in animal agriculture and monitor the emergence and spread of antibiotic-resistant breed human livestock populations in. A single healthcare strategy that effectively and collaboratively addresses infection control can help ensure the availability and efficacy of antimicrobials for many years to come (McEwen & Collignon, 2018).

Known as medicinal plants, preparations derived from the active ingredients of plant parts such as leaves, roots, stems, and flowers, these substances have been investigated for their potential therapeutic value in modern medicine in the 19th century and are commonly used in traditional medicine (Jain et al., 2019). Medicinal plant extracts can contain a wide variety of active compounds, such as terpenes, flavonoids, alkaloids, and other compounds with bioactive properties These molecules can be isolated from plant material and purified for pharmaceutical use and other health care products. They may have anti-inflammatory, anti-inflammatory, anti-inflammatory, or other healing actions (Budovsky et al., 2015). There are several methods of preparing medicinal plants, including solvent extraction, distillation, flotation, and crushing. The resulting juice can be used to make a variety of medicinal products including tablets, capsules, ointments, and teas. You can also take liquid, powder, or dried plant shapes (Rasul, 2018).

Echinacea ssp. is a plant that boosts immune system function and prevents or treats infections (Aucoin et al., 2020), similarly, *Ginkgo biloba* improves memory and cognitive function (Barbalho et al., 2022), St. John's wort, treat mild to moderate depression (Ng et al., 2017), *Turmeric* spp. reduce inflammation (Choi et al., 2019) by acting as an antioxidant and *Valerian* spp. treat anxiety and insomnia (Borras et al., 2021).

While plant extracts have been used in traditional medicine for centuries, it is important to note that not all plant materials are safe or effective for all individuals or health conditions it is always wise to consult with a health professional before using any other herbal or natural remedies (Black et al., 2019).

Nanotechnology can be applied in the manufacturing and delivery of medicinal plant products to improve their stability, potency, and targeted delivery. The active ingredients in plant materials can be effectively encapsulated and delivered with the help of nanoparticles, which in turn allows them to be delivered to certain target cells or tissues (Patra et al., 2018). Nanoparticle-based strategies for the delivery of plant-derived anticancer agents are one example of how nanotechnology has been applied to the isolation of medicinal plants by intentionally targeting cancer cells, nanoparticles can deliver large amounts of active ingredients with few side effects (Patra et al., 2018). For example, curcumin, the anti-cancer component of turmeric, can be encapsulated in nanoparticles, immobilized, and further solubilized, which in turn will facilitate the delivery of the substance, especially to cancer cells (Hardwick et al., 2021).

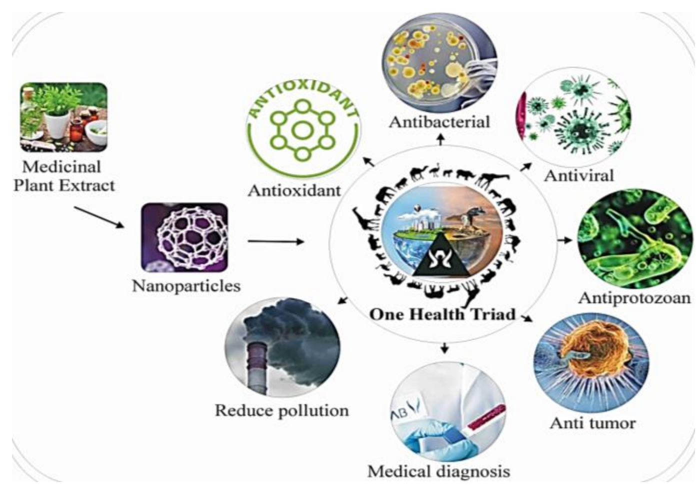

Fig 1. Application of nanotechnology in transport and medicinal plants for pharmaceutical purposes (Khan and Gurav, 2018) i.e antioxidant (Borras et al., 2021), antibacterial (Jun et al., 2011), antiviral, antiprotozoan, Antitumor (Liu, H et al 2013), medical diagnosis and reduce pollution (Gonelimali et al., 2018).

Another application of nanotechnology is to enhance the extraction and purification of active ingredients from medicinal plants (Fig. 1). To purify active chemicals in plant materials and improve yields, nanoporous materials such as zeolites and mesoporous silica can be used for specific selectivity and separation (Iqbal & Umar, 2019). Moreover, nanotechnology can be used to develop unique plant-based nanomedicines for the treatment of various diseases (Khan & Guruv, 2018). For example, nanoparticles loaded with plant extracts can be used as drug delivery vehicles or wound dressings for the treatment of inflammatory diseases such as rheumatoid arthritis (Rahimi et al., 2021). The use of nanotechnology for the pharmaceutical formulation of plant extracts can improve the therapeutic properties of these natural remedies and enhance their safety and effectiveness for the treatment of various diseases (Patra et al., 2018).

Nanoparticles or particles smaller than 100 nanometers have unique chemical properties that make them useful for disinfection one of the main advantages of nanoparticles is their high surface-to-volume ratio, allowing them to interact with bacterial cells better communication. In addition to being able to communicate as highly effectively in bacterial cells, nanoparticles can deliver multifunctional drugs such as antibiotics due to their higher surface area than traditional materials (Jun et al., 2011; Theivasanthi & Alagar, 2011; Khorasany & Hosseinzadeh, 2016).

One of the most extensively studied types of nanoparticles for antimicrobial activity is silver nanoparticles. It has been shown to inhibit the growth of various bacteria including Gram-positive and Gram-negative bacteria. The bactericidal properties of silver nanoparticles are explained by their ability to damage the cell membrane by breaking down the bacterial cell wall, eventually inducing bacterial death to further enhance its bactericidal effect (Li et al., 2010; Le Ouay & Stellacci, 2015; Rajeshkumar & Bharath, 2017; Tang & Zheng, 2018).

Other types of nanoparticles, such as titanium dioxide and zinc oxide, have also been investigated for their antibacterial properties. These nanoparticles generate reactive oxygen species (ROS), which damage bacterial membranes, proteins, and DNA. It is commonly used to create durable antimicrobial protection for various products such as textiles, coatings, and medical devices (Ann et al., 2014; Nandhini et al., 2019; Balalakshitha et al., 2021; Al Jabri et al., 2022; Thiruchelvi et al., 2022).

Although nanotechnology has shown great promise for antimicrobial activity, there are some risks and issues. For example, because nanoparticles are small, they can accumulate in tissues and cross biological barriers such as the blood-brain barrier, which can cause side effects and undetectable interactions of nanoparticles with proteins and biomolecules others have as well. Consequently, in order to completely comprehend the possible hazards and advantages of nanotechnology in antimicrobial activities (Fig. 2), study and testing must continue (Abdallah et al., 2020; Dasauni et al., 2021; Paiva-Santos et al., 2021; Farooq et al., 2022; Habeeb et al., 2022; More et al., 2022; Yang et al., 2022).

THE ANTIMICROBIAL CHARACTERISTICS OF EXTRACTS FROM MEDICINAL PLANTS

Crude extracts from the root, stem, flower, fruit, and twigs of medicinal plants were widely used in traditional medicine to treat a variety of human illnesses (Khan et al., 2013Medicinal plants include a variety of phytochemicals, such as flavonoids, alkaloids, tannins, and terpenoids, that have antibacterial and antioxidant properties. The antibacterial qualities of some plant species have been thoroughly investigated. For example, crude extracts of curry, ginger, garlic, sage, mustard, curry, and other herbs can inhibit a range of Gram-positive and Gram-negative bacteria (Khan et al., 2018; Castro et al., 2008). Furthermore, it has been shown that the growth of Escherichia coli and other germs during the preservation of meat, juices, and milk may be successfully inhibited by extracts from Chinese chives and cassia. In a related research (Doddanna et al. , 2013) examined how various plant extracts affected Candida albicans growth. The findings showed that curry leaf alcoholic extract successfully inhibited C. albicans growth with 24.05 0.07 after 48 hours. Additionally (Mwitari et al., 2013) shown that thyme oil extract might inhibit the development of Pseudomonas

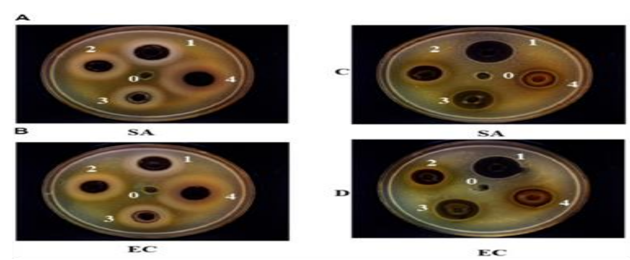

Fig 2. The 20% (w/v) inhibitory zone of aqueous and ethanolic extracts (C,D) of rosemary (3), clove (1), thyme (4), and escerichia coli (EC) against Staphylococcus aureus (SA) strains of bacteria. 10% v/v DMSO for ethanolic extracts and distilled water for aqueous extracts are represented by the numbers (0), which represents the negative control.

aeruginosa and Candida albicans.

ANTIMICROBIAL ACTION OF MEDICINAL PLANTS

In order to maximize the use of medicinal plant extracts as natural antibacterial agents to prolong shelf life and preserve food quality, it is necessary to first understand the mechanism of action of these extracts. To that end, the present study aims to: (1) compare the efficacy of two extraction techniques, namely conventional extraction and ultrasound techniques; (2) investigate the antimicrobial activity of ethanolic and water extracts of roselle (*Hibiscus sabdariffa*), rosemary (*Rosmarinus officinalis*), clove (*Syzygium aromaticum*), and thyme (*Thymus vulgaris*) against seven common food pathogens and spoilage microorganisms; and (3) comprehend the mechanisms of action of the tested plant extracts in relation to possible disruption of the membrane of microorganisms and modifications in cytoplasmic pH. (Gonelimali et al., 2018).

EXAMPLES OF MEDICINAL PLANT EXTRACTS WITH ANTIBACTERIAL ACTIVITY

The ginger root (genus *Zingibe*r) is widely used in medicine to treat a variety of illnesses, including rheumatoid arthritis, diabetes, xerostomia, nausea, vomiting, motion sickness, gastrointestinal ulcers, dry mouth, cancer, migraine headaches, sore throats, and minor respiratory ailments. *Zingiber offcinale* Roscoe, or ginger, is a member of the Zingiberaceae family. (Kadnur & Goyal, 2005). Ginger is most often recognized in Spanish as Gengibre or Ancoas, while in Pakistan, it's called "Adrac." (Ravindran & Babu, 2004).

Many bacterial infections have evolved multiple drug resistance (MDR) as a result of the widespread use of antibiotics. The current study examined the in vitro antibacterial activity of a few common culinary spices from Pakistan against clinically significant bacterial infections (Yuan et al., 2011). One of the most often used culinary ingredients and spices in everyday home cooking is the plant's horizontally solid subterranean stem, or rhizome, which has a gracefully coated skin (Lantz et al., 2007). In addition to being used as a flavoring, ginger is valued in allopathic, tibbe-e-unani, and ayurvedic medicine (Fessenden et al., 2001), home medications, and aromatherapy (Sloand & Vessey, 2001). Ginger rhizome can be used to make dry powder, preserved slices, fresh paste, and ginger tea (flavoring) (El-Ghorab et al., 2010).

TRADITIONAL MEDICINAL USE OF PLANTS IN ANTI-INFECTIOUS PRACTICES

In the Pteridaceae family, *Adiantum capillus-veneris* L. is a common fern found in the Himalayan region's damp temperate climate. urinary tract infections (UTIs) are frequently treated with it as an aqueous infusion. It also functions as a diuretic, astringent, demulcent, and antitussive (Ishaq et al., 2014).

A paste made from the aerial portions of *Artemisia absinthium* L. (Asteraceae) is applied topically to treat inflammatory and infectious skin problems, as well as itch. Many *Artemisia* species have been used traditionally, and some have even been used to generate medications to treat typhoid and malaria (Hayat et al., 2009). A thorny plant of the Berberidaceae family, *Berberis lycium* Royle has long been used to cure piles, cholera, and diarrhea. Diarrhea, internal wounds, shattered bones, diabetes, jaundice, and eye infections are among the signs. Traditionally, bark infusions have been used to treat toothaches, earaches, and oral infections. (Abbasi et al., 2010).

Within the Rosaceae family, *Pyrus pashia* Buch. -Ham. ex D. Don is a woody shrub that bears edible fruit. It is used topically to treat respiratory, cardiovascular, and gastrointestinal conditions as well as to act as a laxative (Janbaz et al., 2015). Locals frequently employ the entire plant infusion of *Swertia chirata* Buch. -Ham. ex C.B. Clarke, to cure hepatitis, inflammation, and digestive disorders. It is also used for bronchial infections, skin conditions, malaria, and persistent fever (Kumar & Van Staden, 2016). The Rutaceae family plant *Zanthoxylum armatum* DC., sometimes referred to as "timber," has been utilized as a chewing stick by the locals to heal oral sores and dental diseases. According to reports, the plant's fruits and bark are also used to cure cancer and digestive issues including cholera and dysentery (Tuchscherer et al., 2014).

NANOPARTICLES WITH ANTIBACTERIAL ACTIVITY

There are several biologically active inorganic nanoparticles found in the human body i.e., zinc, copper, iron, magnesium, cobalt, etc. By using various chemical and physical methods these metals are manufactured in the form of nanoparticles. Physiologically significant nanoparticles are still investigated for their application in different fields as well as for therapeutics. The effectiveness of nanoparticles in medical applications is determined by their size and composition. A key feature of nanoparticles is that they can target a variety of bacterial structures. Some of the nanoparticles with antibacterial activity are explained below (Sengupta et al., 2014).

SILVER NANOPARTICLES (Ag NPs)

Silver has been used alone or in combination with other technologies, as an antibiotic. As it is evident from research silver possesses antibacterial activities. As antibiotic resistance is a matter of global concern, silver nanoparticles appear as a magnificent alternative to the diseases caused by antibiotic-resistant bacteria. Silver nanoparticles show their antibiotic action through different mechanisms of action, which able them to penetrate and attack multiple structures of microorganisms.

Three mechanisms have been postulated for the antimicrobial action of silver nanoparticles:

AgNPs accumulate inside the cell membrane, and destabilize it which causes the leaking of cellular contents and ultimately leads to cell death. They also cause cell wall rupturing by interacting with the proteins containing sulfur group present in the cell wall. AgNPs produce reactive oxygen species and free radicals by interfering with the enzymes having a thiol group, The apoptosis pathway is activated this way and causes damage to the intracellular machinery, which may interfere with the oxygen-carrying capacity inside the membrane. Literature also supports another mechanism that runs parallel with these two mechanisms: the liberation of silver ions. When exposed to Ag ions, the bacteria's DNA conglomeration defense mechanisms defend them from the harmful environment, but the potential of bacteria replication is affected. Thus, the responses to silver ions and nanoparticles vary, but both of them are necessary to fully understand the antibacterial activity of AgNPs (Seil & Webster, 2012).

ZINC OXIDE NANOPARTICLES (ZnO NPs)

It is reported that ZnO NPs exhibit broad-spectrum antibacterial action against a variety of pathogenic bacteria, including *Pseudomonas aeruginosa*, *Mycobacterium* TB, *Bacillus subtilis*, *Klebsiella aerogenes*, and *Staphylococcus aureus*. In contrast with soluble zinc compounds like zinc chloride, a better antibacterial activity is shown by ZnO nanoparticles due to their potential to disrupt the cell membrane actively. Internalization of ZnO nanoparticles, enzyme inhibition, and generation of reactive oxygen species are considered the main mechanisms of the antibacterial action of Zinc oxide nanoparticles (Agarwal et al., 2018). Gram +ve and gram -ve bacteria show different mechanisms of attachment of zinc particles due to the structure difference of their cell membranes. Gram +ve bacteria are less susceptible to nanoparticle toxicity in comparison to Gram -ve bacteria because gram +ve has a thick layer of peptidoglycan which exhibits more resistance to nanoparticle contact with the cell membrane. Zinc oxide nanoparticle ions are transferred inside the cell membrane through porins. Zn ions are passively diffused through these porins inside the cell where ZnO dissolves in the aqueous medium and releases Zn+ ions. Zn+ ions get self-attached to the membrane due to the electrostatic force of attraction as the membrane is negatively charged (Patra et al., 2017).

Zinc oxide produces hydroxyl ion OH^-, superoxide ion O_2^{-}, peroxide H_2O_2, and singlet oxygen. As Hydroxyl ions and superoxide ions are negatively charged, therefore, they are unable to penetrate the bacterial cell membrane but peroxide ions perforate easily and disrupt the cell membrane (Von Moos & Slaveykova, 2014). Instant oxidative stress further damages the DNA, lipids, and proteins. When DNA is damaged, cells typically attempt to repair it to avoid apoptosis or necrosis. If the cell is unable to successfully repair the damaged DNA, it may ultimately undergo programmed cell death or necrosis (Leung et al., 2016)

COPPER NANOPARTICLES (Cu-NOPs)

The bactericidal action of copper nanoparticles is dependent on ions concentration, at low concentration Copper acts as a micronutrient to bacteria while at high concentration these ions act as bactericidal. Copper disrupts the bacterial cell membrane in several ways, microorganisms are unable to resist the multiple mechanisms of copper ions occurring simultaneously (Raffi et al., 2010). The bactericidal action of copper nanoparticles is initiated by the adsorption of copper ions onto the bacterial cell surface, this enhances the permeability of the membrane and leakage of cellular contents. It also interferes with the oxygen-carry capacity of the bacterial cell by altering the enzyme's function required for the metabolism of oxygen to live, all of these events lead to cell death (Selvarani, 2018). Hydrogen peroxide is produced by a redox reaction between Cu^{2+} and Cu ions which destabilizes the bacterial cell membrane and causes toxicity to bacteria.

IRON OXIDE (Fe_3O_4-NPs)

Iron oxide nanoparticles gain attention because they are cost-effective, easy to synthesize in the laboratory, physically and chemically stable also biocompatibility, and environment friendly. These nanoparticles damage the cell membrane either by producing reactive oxygen species or directly attaching to the lipid molecules of bacterial cells as a result bacterial cell membrane is damaged and this leads to the influential bactericidal effect of iron oxide nanoparticles (Ansari et al., 2017).

GOLD NANOPARTICLES (AuNPs)

Due to their strong bactericidal properties, gold nanoparticles are effective in eliminating bacteria. Their well-developed surface chemistry, chemical firmness, and small size make them trouble-free from interfering with microorganisms. The difference in the sensitivity of various strains of bacteria i.e. gram-positive and gram-negative is mainly due to the difference in their composition of cell membranes, metabolism, and their interaction with nanoparticles.

The electrostatic interaction between negatively charged microcells and positively charged gold can give AuNPs a bactericidal effect on bacteria Small AuNPs have the ability to penetrate bacterial cells, disrupt cell wall integrity, and ultimately infect cells degradation of AuNPs release gold ions, giving them antibacterial properties. Increasing the surface area and number of particles (SSA) can enhance the penetration of AuNPs into cell membranes and enhance their antimicrobial activity intermediately (Bindhu & Umadevi, 2014).

The antimicrobial ability of nanoparticles is greatly influenced by their size and concentration. The main reason why AuNPs have strong antibacterial properties is due to their high surface reactivity (López-Miranda et al., 2019). AuNPs are safer than other nanoparticles due to their ROS-inactive mode of action (Tiwari et al., 2011).

ADVANTAGES

Gram-positive, Gram-negative, and resistant strains were among the many strains for which nanoparticles exhibited antimicrobial activity. By using nanoparticles, adverse effects are reduced since a lower standard dosage is needed to provide an effective antibacterial activity against certain bacterial strains.

Nanoparticles, due to their small size, can easily cross the different membrane barriers and penetrate individual cells. This helps to achieve personalized medicine by targeting the site of action with the use of nanotechnology, this maximizes the therapeutic effects while minimizing the effects on other sites of action. Nanoparticles can also serve as a carrier for drugs and antibiotics by making complex with them thus improving their release and selectivity. Nanoparticles also enhance the antibacterial effect of other drug molecules. Nanoparticles are also used as drug delivery agents i.e., in cancer therapy, and MRI contrast agents (Dobson, 2010). The broad spectrum of bioactivity of nanoparticles makes them auspicious agents not only to fight infections but also in distinct biomedical areas (Franci et al., 2017).

DISADVANTAGES

Nanoparticles have become a popular subject of research and development in various fields, including medicine, electronics, and energy. However, the use of nanoparticles also raises concerns about their potential negative impacts on human health and the environment. Here we explore the disadvantages of using nanoparticles, including their potential toxicity, environmental impact, and ethical considerations. Through an academic and informative approach, we provide a comprehensive understanding of the menace corresponding with the use of nanoparticles.

ZnO Nps are extensively utilized in various industries such as electronics, textiles, and rubber as well as in medicine for their antimicrobial and anti-inflammatory properties. Additionally, they are widely used in cosmetics, bio-imaging, drug delivery, and photocatalysis. Consequently, humans are frequently exposed to these NPs, which increases the risk of exposure (Vandebriel & De Jong, 2012). Zinc oxide nanoparticles have been found to be highly toxic if inhaled. These nanoparticles can enter the lung tissue by passing through alveolar epithelial cells, leading to a serious inflammatory response in the lungs (Liu et al., 2013). However, NPs, which are very small in size like viruses, can stimulate the activation of different inflammatory biomarkers i.e. growth factor-β1 (TGF-β1), tumor necrosis factor-α (TNf-α), and interleukins (IL) which trigger the series of immune reactions and harmful events like fibrosis and pulmonary inflammation.

Studies have shown that repeated administration of carbon nanotubes in male mice can induce reversible harm to the testes. Additionally, a recent report in Nature Nanotechnology by Kalan found that pregnant mice treated with silica nanoparticles of 70 nm diameter and titanium dioxide of 35 nm suffered damage to the placenta and fetus, leading to serious pregnancy complications in mice. These findings highlight the need for careful consideration of the teratogenic toxicity exhibited by these particles before they are incorporated into everyday medical and consumer products. Exposure to nanoparticles can pose significant health risks to humans. To mitigate these risks, it is important to employ chemical approaches such as surface treatment, functionalization, and composite formation to address issues related to toxicity (Singh et al., 2013).

COMBINATION OF NANOTECHNOLOGY AND MEDICINAL PLANTS

In healthcare, medicinal plants are a good source of reducing symptoms or treating fever and other diseases. Medicinal plants have important antimicrobial properties which make them useful for future discovery of antibiotics (Sofowora et al., 2013). In herbal formulation, there are many active compounds and their stability should also be determined. Patients have more confidence in medicines that have stable flavonoids, tannins, and terpenoids are natural active compounds in the extracts of herbal medicines. These are soluble in water but they cannot cross lipid membranes so they are less absorbable. Due to the large size of the molecule, they have less bioavailability and effectiveness. Due to these types of issues, some extracts cannot be used for medicinal purposes. To overcome the issue, a blend of herbal drugs with nanotechnology is highly recommended (Tungmunnithum et al., 2018).

Herbal extracts are more effective when prepared using a nanostructured method. Additionally, it lessens the need for dosage, minimizes negative effects, and increases activity (Bonifácio et al., 2014). Throughout the treatment duration, nanotechnology supplies the ingredients at the site where it is required and also keeps their concentration adequate. Improved bioavailability, stability, and solubility, reduced toxicity, enhanced biological activity, tissue macrophage dispensation, controlled distribution, inhibition of physical and chemical changes, and disintegration are among the primary benefits (Dewi et al., 2022).

A study investigated the efficacy of extracts from *A. heirochuntica* and *A. absinthium* as mediators in the synthesis of AgNP, as well as the antibacterial and anticandidal properties of the AgNP. For the fabrication of AgNP, an aqueous extract of *A. heirochuntica* and *A. absinthium* was used. Bacitracin (BA), ciprofloxacin (CI), cefixime (CE), and tetracycline (TE) are the standards and the activity of An-AgNP was compared to these standard microbes. Its activity was more than all of the antibiotics which are tested against *E. coli* and *S. aureus*. P. aeruginosa was observed with the same activity except for BA which has higher activity than An-AgNP. AgNP showed less activity for C.albicans than metronidazole and fluconazole (Aabed & Mohammed, 2021).

the use of nanotechnology to enhance the efficacy of antimicrobial plants is a real strategy to discover in the fight against infectious diseases(Castillo-Henríquez et al., 2020).

Due to their unique biochemical properties, selenium particles known as selenium nanoparticles (SeNPs) are desirable

Tab 2. Synthesis and characterization of herbal nano-suspensions for enhanced therapeutic efficacy.

Medicinal Plants Name	Nanoparticles	Dosage	Model	Mechanism	Overall effects	References
Ethanolic roselle extract	-	10 g	*In-vitro*	↑ Cell membrane disturbance	Antibacterial	Gonelimali et al., 2018
Biebresteinia multifida *Polypodium vulgare*	-	1.28 ng/ml 63.48 ng/ml	*In-vitro*	↑ free radical scavenging	Antioxidant	Xu et al., 2017
Ocimum Sanctum (Tulsi) leaf extracts	Silver Nanoparticles (AgNPs)	82.02 ± 8.17 mg	*In-vitro*	↑ DNA damage ↑ ROS production	Antibacterial	Jain et al., 2017
A. indica and *A. lanata* extracts	-	5, 10, 20 and 30 µg	*In-vitro*	↑ Protein denaturation	Antibacterial	Mickymaray et al., 2016
Phytoconstituents	Copper Nanoparticles	20 g of the powdered leaves	*In-vitro*	↓ *E. coli* ↓ *P. aeruginosa*, ↓ *S. aureus*, ↓ *B. subtilis*	Antibacterial	Murthy et al., 2020
Medicinal plants leaf extract	Sulphur Nanoparticles	200 µg/ml	*In-vitro*	↓ *E. coli* ↓ *S. aureus*	Antibacterial	Paralikar et al., 2018
I. balsamina and *L. camara* leaf extracts	-	3 mM - 5 mM Ag	*In-vitro*	↓ Growth of *E. coli* ↓ Growth of *S. aureus*	Antibacterial	Aritonang et al., 2019
Desmodium gangeticum (Linn.), *Eclipta alba* (Linn.), *Ocimum sanctum* (Linn.), *Piper longum* (Linn.), *Solanum nigrum* (Linn.) and *Amaranthus caudatus* (Linn.) extracts	-	3.86 ± 0.20 - 21.33 ± 1.49 mg/100g	*In-vitro*	↓ Oxidative stresss ↓ *A. caudatus* ↓ *S. nigrum* ↓ *P. longum* ↓ *E. alba* ↓ *O. sanctum*	Antioxidant Antimicrobial	Lee et al., 2003
Terminallia chebula, *Terminallia bellerica*, *Phyllanthus emblica*, *Punica granatum*, *Lawsonia alba* and *Mikania micrantha*	-	2000 µg/ml	*In-vitro*	↓ *S. aureus* MTCC 2940 ↓*B. subtilis* MTCC 441 ↓ *E. coli* MTCC 739 ↓ *P. vulgaris* MTCC 426 ↓ *E. aerogenes* MTCC 111	Antimicrobial	Ghosh et al., 2008

Mixed solutions of An-AgNPs with ciprofloxacin, tetracycline, cefixime, or bacitracin showed abundant synergistic effects against *E. coli* in comparison to the antibiotic's action alone (Cunha et al., 2016). Simple, low-cost, non-toxic, and reproducible green compounds can be AgNPs with high antimicrobial efficiency, as shown in studies elsewhere where AgNPs were found to be carriers trap is stable, and the FTIR results indicated that phytochemicals can play an important role in reducing and stabilizing the presence of AgNPs (Lediga et al., 2018).

AgNPs synthesized with extracts of *S. birrea* and *E. autumnalis* also showed strong antimicrobial activity against both Gram-positive and Gram-negative bacteria (Deng et al., 2016). Toxicity of *S. birrea* and *E. autumnalis*-AgNPs was found to be minimal and non-existent. These results suggest that

for commercial and various biological products can synthesize SeNPs by chemical methods, such as sodium borohydride (NaBH4) subjected to fire or explosion (Xia et al., 2022). Thus, SeNPs generated through chemistry must be carefully monitored and controlled to avoid any adverse effects on the environment or human health In contrast, SeNPs generated by biosynthesis are a more ecologically benign process. Biosynthesis using plant materials produces SeNPs without hazardous compounds that could pose a threat to the environment (Pyrzynska & Sentkowska, 2022).

In addition, plant materials are easily accessible, durable, and renewable, making the biosynthesis of SeNPs a potentially economically viable option In conclusion, chemical synthesis of SeNPs lies ahead ara is a widely used method, but it can be hazardous and must be handled with caution to avoid adverse effects on the environment and human health. Biosynthesis using plant materials provides an alternative low-risk potentially expensive and environmentally friendly. The creation of affordable and sustainable technologies depends on the efficient use of available resources (Ikram and Javed, 2021).

Boldo, onion, and acerola plants, which are readily available and commonly found in Brazilian markets and households, were selected by the researchers who conducted this study. The study also found that onions and boldo are rich in quercetin, a flavonoid that has shown antimicrobial activity against some Gram-positive bacteria. These results suggest that the plant extracts under study may be useful as natural antibiotics. Previous studies have shown that purified quercetin can effectively stabilize SeNPs by chemical synthesis, which is S. aureus (Souza et al., 2022).

Consequently, the addition of quercetin and boldo from onion to the biosynthesis of the SeNPs can improve the stability and antibacterial potential of the final nanoparticles Improving the stability and bactericidal potential of s can (Gunti et al., 2019). Acerola is rich in ascorbic acid, a reducing agent required in the synthesis of many important metabolic processes (Prakash and Baskaran, 2018). When Vahdati and Moghaddam (2020) synthesized SeNPs with ascorbic acid in a previous study. This suggests that ascorbic acid from acerola can also be used as a reducing agent for the formation of SeNPs. Furthermore, previous studies have shown that several chemicals in the extracts used in this study are effective in producing SeNPs and exhibit their antibacterial properties (Hassan et al., 2022). As a result, the synthesis of SeNPs relies on a mixture of different plant materials to provide reducing molecules and potentially increase stability levels c10a, c20a, b10a, and b20a, synthesized SeNPs at work of these showed bactericidal activity against many tested pathogens, including *S .aureus*, MRSA, and *S. agalactiae* Only the Gram-positive strains studied showed bactericidal activity (Han & Patel, 2021).

In summary, ascorbic acid from acerola is a good reagent that can contribute to the production of SeNP by acting as a reducing agent. During the synthesis of SeNPs, the combination of various plant extracts can enhance the antimicrobial activity. Against some Gram-positive pathogens, the SeNPs synthesized in this work showed antimicrobial activity, indicating their potential use in antibiotics (Salem & Badawy, 2022).

CONCLUSION

In medicine, nanotechnology has shown great promise, including new drug development and drug delivery methods. Enhancement of the antimicrobial properties of medicinal plant materials using nanotechnology is an exciting new direction in antimicrobial therapy This can reduce human resistance to antibiotics of the plant, increase the potency and selectivity of the plant, and provide a long-term, affordable solution to the growing issue of infectious disease further research is needed to provide have been quantified and widely applied in nanotechnology This single-health approach provides a viable alternative to traditional antibiotics and is an important step against antibiotic resistance worldwide.

REFERENCES

Aabed K & AE Mohammed, 2021. Synergistic and antagonistic effects of biogenic silver nanoparticles in combination with antibiotics against some pathogenic microbes. Frontiers in Bioengineering and Biotechnology 9:12-25.

Abbasi AM, MA Khan, N Khan & MH Shah, 2013. Ethnobotanical survey of medicinally important wild edible fruits species used by tribal communities of Lesser Himalayas-Pakistan. Journal of Ethnopharmacology 148:528-536.

Abdallah Y, M Liu, SO Ogunyemi, T Ahmed, H Fouad, A Abdelazez, C Yan, Y Yang, J Chen & B Li, 2020. Bioinspired green synthesis of chitosan and zinc oxide nanoparticles with strong antibacterial activity against rice pathogen Xanthomonas oryzae pv. oryzae. Molecules 25:47-95.

Agarwal, H, Menon S, Kumar SV & S Rajeshkumar, 2018. Mechanistic study on antibacterial action of zinc oxide nanoparticles synthesized using the green route. Chemico-Biological Interactions 286:60-70.

Al Jabri H, M H Saleem, M Rizwan, I Hussain, K Usman & M Alsafran, 2022. Zinc oxide nanoparticles and their biosynthesis: overview. Life 12:594.

Ali H & Qaiser, 2009. The ethnobotany of Chitral valley, Pakistan with particular reference to medicinal plants. Pakistan Journal of Botany 41:2009-2041.

Ann LC, S Mahmud, SKM Bakhori, A Sirelkhatim, D Mohamad, H Hasan, A Seeni & RA Rahman, 2014. Antibacterial responses of zinc oxide structures against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Streptococcus pyogenes*. Ceram International 40:2993–3001.

Ansari SA, M Oves, R Satar, A Khan, SI Ahmad, MA Jafri, SK Zaidi & MH Alqahtan, 2017. Antibacterial activity of iron oxide nanoparticles synthesized by co-precipitation technology against *Bacillus cereus* and *Klebsiella pneumonia*. Polish Journal of Chemical Technology 19:110-115.

Aucoin M, K Cooley, PR Saunders, J Care, D Anheyer, DN Medina, V Cardozo, D Remy, N Hannan & A Garber, 2020. The effect of *Echinacea* spp. on the prevention or treatment of COVID-19 and other respiratory tract infections in humans: A rapid review. Advanced Integrated Medicine 7:203–217.

Balalakshitha M, K Kolanjinathan, T Aishwarya & B Vinothini, 2021. A Review on diabetic wound infection and its treatment using zinc oxide nanoparticle synthesized by green chemistry techniques. Environmental Pharmacology Life Science 10:1–22.

Barbalho SM, R Direito, LF Laurindo, LT Marton, EL Guiguer, RA Goulart, RJ Tofano, ACA Carvalho, UAP Flato & VAC Tofano, 2022. *Ginkgo biloba* in the aging process: A narrative review. Antioxidants 11:525.

Begum S, T Begum, N Rahman & RA Khan, 2021. A review on antibiotic resistance and way of combating antimicrobial resistance. GSC Biology Pharmacology Science 14:87–97.

Bindhu MR and MJML Umadevi, 2014. Antibacterial activities of green synthesized gold nanoparticles. Materials Letters 120:122-125.

Black N, E Stockings, G Campbell, LT Tran, D Zagic, WD Hall, M Farrell & L Degenhardt. 2019. Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. The Lancet Psychiatry 6:995–1010.

Bonifacio BV, PB Silva, MA Ramos, KM Negri, TM Bauab & M Chorilli, 2014. Nanotechnology-based drug delivery systems and herbal medicines: A review. International Journal of Nanomedicine. 9:1-15.

Bonilla-Aldana DK, K Dhama & AJ Rodriguez-Morales, 2020. Revisiting the one health approach in the context of COVID-19: a look into the ecology of this emerging disease. Advance Animal Veterinary Science 8:234–237.

Borras S, I Martínez-Solis and JL Rios, 2021. Medicinal plants for insomnia related to anxiety: an updated review. Plant Medicine 87:738–753.

Budovsky A, L Yarmolinsky & S Ben-Shabat, 2015. Effect of medicinal plants on wound healing. Wound Repair Regeneration 23:171–183.

Buregyeya E, E Atusingwize, P Nsamba, C Nalwadda, J Osuret, P Kalibala, R Nuwamanya, S Okech, T Ssekamatte and & S Nitumusiima, 2021. Lessons from a community based interdisciplinary learning exposure: benefits for both students and communities in Uganda. BMC Medicine Education 21:1–13.

Castillo-Henriquez L, K Alfaro-Aguilar & J Ugalde-Álvarez. 2020. Green synthesis of gold and silver nanoparticles from plant extracts and their possible applications as antimicrobial agents in the agricultural area. Nanomaterials 10:250-270.

Castro SBR, CAG Leal, FR Freire, DA Carvalho , DF Oliveira & HCP Figueiredo, 2008. Antibacterial activity of plant extracts from Brazil against fish pathogenic bacteria. Brazilian Journal of Microbiology. 39:756-760.

Choi Y, I Ban, H Lee, MY Baik & W Kim, 2019. Puffing as a novel process to enhance the antioxidant and anti-inflammatory properties of *Curcuma longa* L (turmeric). Antioxidants 8:50-61.

Collignon PJ & SA McEwen, 2019. One health—its importance in helping to better control antimicrobial resistance. Tropical Medicine Infection Disease 4:22-29.

Cunha FA, KR Maia, EJJ Mallman, MCDSO Cunha, AAM Maciel, IPd Souza, EA Menezes & PBA Fechine, 2016. Silver nanoparticles-disk diffusion test against escherichia coli isolates. Revista do Instituto de Medicina Tropical de Sao Paulo. 58:200-209.

Dasauni K, D Bisht & TK Nailwal, 2021. Novel nanotechnology-based approaches in the treatment of leishmaniasis. In: Pathogenesis, Treatment and Prevention of Leishmaniasis (Samant M & SC Pandey ed.). Elsevier, London, UK. pp:125–140.

De Garine-Wichatitsky M, A Binot, J Ward, A Caron, A Perrotton, H Ross, H Tran Quoc, H Valls-Fox, IJ Gordon & Promburom, 2021. “Health in” and “Health of” social-ecological systems: A practical framework for the management of healthy and resilient agricultural and natural ecosystems. Frontior Public Healing 8:616328.

Deng H, D McShan, Y Zhang, SS Sinha, Z Arslan, PC Ray & H Yu, 2016. Mechanistic study of the synergistic antibacterial activity of combined silver nanoparticles and common antibiotics. Environmental Science and Technology 50:8840-8848.

Destoumieux-Garzon D, P Mavingui, G Boetsch, J Boissier, F Darriet, P Duboz, C Fritsch, P Giraudoux, F Le Roux and S Morand. 2018. The one health concept: 10 years old and a long road ahead. Frontior Veterinary Science 14:202-215.

Dewi MK, AY Chaerunisaa, M Muhaimin & IM Joni, 2022. Improved activity of herbal medicines through nanotechnology. Nanomaterials 12:40-73.

Dhingra AK, B Chopra & SK Mittal, 2013. *Martynia annua* L.: a review on its ethnobotany, phytochemical and pharmacological profile. Journal of Pharmacognosy and Phytochemistry 1:135-140.

Dobson J, JK Patra, K Baek, CO Perera, 2017. Antibacterial activity and synergistic antibacterial potential of biosynthesized silver nanoparticles against foodborne pathogenic bacteria along with its anticandidal and antioxidant effects. Frontiers in Microbiology 8:1–14.

Doddanna SJ, S Patel, MA Sundarrao & RS Veerabhadrappa, 2013. Antimicrobial activity of plant extracts on *Candida albicans*: An in vitro study. Indian Journal of Dental Research 24:401.

Dugassa J & N Shukuri, 2017. Review on antibiotic resistance and its mechanism of development. Journal Healing Medicine Nurse 1:1–17.

El-Ghorab AH, M Nauman, FM Anjum, S Hussain & M Nadeem, 2010. A comparative study on chemical composition and antioxidant activity of ginger (*Zingiber officinale*) and cumin (*Cuminum cyminum*). Journal of Agricultural and Food Chemistry, 58:8231-8237.

Farooq MA, F Hannan, F Islam, A Ayyaz, N Zhang, W Chen, K Zhang, Q Huang, L Xu & Zhou, 2022. The potential of nanomaterials for sustainable modern agriculture: present findings and future perspectives. Environmental Science Nano 9:1926–1951.

Fessenden JM, W Wittenborn & L Clarke, 2001. *Gingko biloba*: a case report of herbal medicine and bleeding postoperatively from a laparoscopic cholecystectomy. The American Surgeon 67:33-35.

Franci G, A Falanga, S Galdiero, L Palomba, M Rai, G Morelli & M Galdiero, 2015. Silver nanoparticles as potential antibacterial agents. Molecules 20:8856-8874.

Ghosh A, BK Das, A Roy, B Mandal, G Chandra, 2008. Antibacterial activity of some medicinal plant extracts. Journal of Natural Medicine 62:259–262.

Gonelimali FD, J Lin, W Miao, J Xuan, F Charle, M Chen & SR Hatab, 2018. Antimicrobial properties and mechanism of action of some plant extracts against food pathogens and spoilage microorganisms. Frontiers in Microbiology 9:1639.

Gonelimali FD, J Lin, W Miao, J Xuan, F Charles, M Chen, SR Hatab, 2018. Antimicrobial properties and mechanism of action of some plant extracts against food pathogens and spoilage microorganisms. Frontiers in Microbiology 9:1–9.

Gunti L, RS Dass & NK Kalagatur, 2019. Phytofabrication of selenium nanoparticles from emblica officinalis fruit extract and exploring its biopotential applications: Antioxidant, antimicrobial, and biocompatibility. Frontiers in Microbiology 10:931.

Habeeb HB, R Dhandapani, S Narayanan, V Palanivel, R Paramasivam, R Subbarayalu, S Thangavelu & S Muthupandian, 2022. Medicinal plants mediated the green synthesis of silver nanoparticles and their biomedical applications. IET Nanobiotechnology 16:115–144.

Han HW & KD Patel, 2021. Selenium nanoparticles as candidates for antibacterial substitutes and supplements against multidrug-resistant bacteria. Biomolecules 11:202-250.

Hardwick J, J Taylor, M Mehta, S Satija, KR Paudel, PM Hansbro, DK Chellappan, M Bebawy & K Dua, 2021. Targeting cancer using curcumin encapsulated vesicular drug delivery systems. Current Pharmacology 27:2–14.

Hassan HU, NI Raja & F Abasi. 2022. Comparative study of antimicrobial and antioxidant potential of *Olea ferruginea* fruit extract and its mediated selenium nanoparticles. Molecules 27:105-109.

Hayat MQ, MA Khan, M Ashraf & S Jabeen, 2009. Ethnobotany of the genus *Artemisia* L. (Asteraceae) in Pakistan. Ethnobotany Research and Applications 7:147-162.

Hussain MA & MS Gorsi, 2004. Antimicrobial activity of *Nerium oleander* Linn. Asian Journal of Plant Sciences 3:177-180.

Ikram M & B Javed, 2021. Biomedical potential of plant-based selenium nanoparticles: A comprehensive review on therapeutic and mechanistic aspects. International Journal of Nanomedicine 16:249-268.

Iqbal M & S Umar, 2019. Nano-fertilization to enhance nutrient use efficiency and productivity of crop plants. Nanomater Plant Potential 20:473–505.

Ishaq MS, MM Hussain,MS Afridi, G Ali , M Khattak & S Ahmad, 2014. In vitro phytochemical, antibacterial, and antifungal activities of leaf, stem, and root extracts of *Adiantum capillus* veneris. The Scientific World Journal 14:16-24.

Jain C, S Khatana & R Vijayvergia, 2019. Bioactivity of secondary metabolites of various plants: a review. International Journal of Pharmacology Science 10:494–504.

Jain S & MS Mehata 2017. Medicinal plant leaf extract and pure flavonoid mediated green synthesis of silver nanoparticles and their enhanced antibacterial property. Scientific Reports 7:1–13.

Janbaz KH, MZ Ahsan, F Saqib, I Imran, M Zia-Ul-Haq, MA Rashid & M Moga, 2015. Scientific basis for use of *Pyrus pashia* Buch.-Ham. ex D. Don. fruit in gastrointestinal, respiratory and cardiovascular ailments. PloS One 10:0118605.

Jun JY, HHNguyen, HS Chun, BC Kang & S Koch, 2011. Preparation of size-controlled bovine serum albumin (BSA) nanoparticles by a modified desolvation method. Food Chemistry 127:1892–1898.

Kadnur SV & RK Goya, 2005. Beneficial effects of *Zingiber officinale* Roscoe on fructose induced hyperlipidemia and hyperinsulinemia in rats Pharmacological Science 25:125-136.

Khan MF, H Tang, JT Lyles, R Pineau, ZUR Mashwani & CL Quave, 2018. Antibacterial properties of medicinal plants from Pakistan against multidrug-resistant ESKAPE pathogens. Frontiers in Pharmacology, 9:815.
Khan T and P Gura, 2018. PhytoNanotechnology: enhancing delivery of plant based anti-cancer drugs. Frontier in Pharmacology. 8:10-22.
Khan UA, H Rahman, Z Niaz, M Qasim, J Khan, Tayyaba & B Rehman, 2013. Antibacterial activity of some medicinal plants against selected human pathogenic bacteria. European Journal of Microbiology and Immunology 3:272-274.
Khorasany AR and H Hosseinzadeh, 2016. Therapeutic effects of saffron (*Crocus sativus* L.) in digestive disorders: a review. Iran Journal Basic Medicine Science 19:455-461.
Kumar V& J Van Staden, 2016. A review of *Swertia chirayita* (Gentianaceae) as a traditional medicinal plant. Frontiers in Pharmacology 6:308.
Lantz RC, GJ Chen, M Sarihan, AM Solyom, SD Jolad & BN Timmermann, 2007. The effect of extracts from ginger rhizome on inflammatory mediator production. Phytomedicine 14:123-128.
Le Ouay B & F Stellacci, 2015. Antibacterial activity of silver nanoparticles: A surface science insight. Nano Today 10:339–354.
Lediga ME, TS Malatjie, DK Olivier, DT Ndinteh & SF van Vuuren, 2018. Biosynthesis and characterisation of antimicrobial silver nanoparticles from a selection of fever-reducing medicinal plants of south africa. South African Journal of Botany. 119:172-180.
Lee SE, HJ Hwang, JS Ha, HS Jeong, JH Kim, 2003. Screening of medicinal plant extracts for antioxidant activity. Life Science 73:167–179.
Leung YH, X Xu, AP Ma, F Liu, AM Ng, Z Shen, LA Gethings, MY Guo, AB Djurisic, PK Lee & HK Lee, 2016. Toxicity of ZnO and TiO2 to *Escherichia coli* cells. Scientific Reports 6(1):35243.
Li WR, XB Xie, QS Shi, HY Zeng, YS Ou Yang & YB Chen, 2010. Antibacterial activity and mechanism of silver nanoparticles on *Escherichia coli*. Apply Microbiology Biotechnology 85:1115–1122.
Liu H, D Yang, H Yang, H Zhang, W Zhang, Y Fang, Z Lin, L Tian, B Lin, J Yan & Z Xi, 2013. Comparative study of respiratory tract immune toxicity induced by three sterilization nanoparticles: silver, zinc oxide, and titanium dioxide. Journal of Hmaterials 248:478-486.
Lopez-Miranda JL, R Esparza, G Rosas, R Perez & M Estevez-Gonzalez, 2019. Catalytic and antibacterial properties of gold nanoparticles synthesized by a green approach for bioremediation applications.Biotechnology 9:1-9.
Marquet K, A Liesenborgs, J Bergs, A Vleugels & N Claes, 2015. Incidence and outcome of inappropriate in-hospital empiric antibiotics for severe infection: a systematic review and meta-analysis. Critical Care 19:1–12.
McCarter YS, 2017. Antibiotics: challenges, mechanisms, opportunities. Journal of Antibiotics 25:256-262.
McEwen SA & PJ Collignon, 2018. Antimicrobial resistance: a one health perspective. Microbiology Spectrum 25:521–547.
Mickymaray S, MS Al Aboody, PK Rath, P Annamalai, T Nooruddin 2016. Screening and antibacterial efficacy of selected Indian medicinal plants, Asian Pacific Journal of Tropical Biomedicine 6:185–191.
More PR, C Zannella, V Folliero, F Foglia, R Troisi, A Vergara, G Franci, A De Filippis & M Galdiero, 2022. Antimicrobial applications of green synthesized bimetallic nanoparticles from *Ocimum basilicum*. Pharmaceutics 14:2457.
Murthy HCA, T Desalegn, M Kassa, B Abebe, T Assefa 2020. Synthesis of green copper nanoparticles using medicinal plant *Hagenia abyssinica* (Brace) JF. Gmel. leaf extract: Antimicrobial Properties. Journal of Nanomater 39:24-81.
Mwitari PG, PA Ayeka, J Ondicho, EN Matu & CC Bii, 2013. Antimicrobial activity and probable mechanisms of action of medicinal plants of Kenya: *Withania somnifera*, *Warbugia ugandensis*, *Prunus africana* and *Plectrunthus barbatus*. PloS One 8:65619.
Nandhini M, SB Rajini, AC Udayashankar, SR Niranjana, OS Lund, HS Shetty & HS Prakash, 2019. Biofabricated zinc oxide nanoparticles as an eco-friendly alternative for growth promotion and management of downy mildew of pearl millet. Crop Protection 121:103–112.
Ng QX, N Venkatanarayanan & CYX Ho, 2017. Clinical use of *Hypericum perforatum* (St John's wort) in depression: A meta-analysis. Journal Infection and Disorder 210:211–221.
Paiva-Santos AC, F Mascarenhas-Melo, SC Coimbra, KD Pawar, D Peixoto, R Cha-Cha, ARTS Araujo, C Cabral, S Pinto & F Veiga, 2021. Nanotechnology-based formulations toward the improved topical delivery of anti-acne active ingredients. Expert Opinion in Drug Delivery 18:1435–1454.
Pal S, YK Tak & JM Song, 2007. Does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the gram-negative bacterium *Escherichia coli*. Applied and Environmental Microbiology 73:1712-1720.
Patra JK, G Das, LF Fraceto, EVR Campos, MP Rodriguez-Torres, LS Acosta-Torres, LA Diaz-Torres, R Grillo, MK Swamy & S Sharma, 2018. Nano based drug delivery systems: recent developments and future prospects. Journal of Nanobiotechnology 16:1–33.
Prakash A & R Baskaran, 2018. Acerola, an untapped functional superfruit: A review on latest frontiers. Journal of Food Science and Technology 55:3373-3384.
Prestinaci F, P Pezzotti & A Pantosti, 2015. Antimicrobial resistance: a global multifaceted phenomenon. Pathology Glob Health 109:309–318.
Pyrzynska K & A Sentkowska. 2022. Biosynthesis of selenium nanoparticles using plant extracts. Journal of Nanostructure in Chemistry 12:467-480.
Raffi M, S Mehrwan, TM Bhatti, JI Akhter, A Hameed & W Yawar, 2010. Investigations into the antibacterial behavior of copper nanoparticles against *Escherichia coli*. Annals of Microbiology 60:75-80.
Rahimi M, G Charmi, K Matyjaszewski, X Banquy and J Pietrasik, 2021. Recent developments in natural and synthetic polymeric drug delivery systems used for the treatment of osteoarthritis. Acta Biomater. 123:31–50.
Rajeshkumar S & LV Bharath, 2017. Mechanism of plant-mediated synthesis of silver nanoparticles–a review on biomolecules involved, characterisation and antibacterial activity. Chemico-Biological Interaction 273:219–227.
Rasul MG, 2018. Conventional extraction methods use in medicinal plants, their advantages and disadvantages. International Journal of Basic Science and Applied Compouting 2:10–14.
Ravindran PN, GS Pillai & KN Babu, 2004. Under-utilized herbs and spices. In: Handbook of herbs and spices (Peter KV ed.). Woodhead Publishing, Nw York, USA, pp:53-103.
Riaz H, A Begum, SA Raza, ZUD Khan, H Yousaf & A Tariq, 2015. Antimicrobial property and phytochemical study of ginger found in local area of Punjab, Pakistan. International Current Pharmaceutical Journal 4:405-409.
Salem SS & M Badawy 2022. Green biosynthesis of selenium nanoparticles using orange peel waste: Characterization, antibacterial and antibiofilm activities against multidrug-resistant bacteria. Life 12:202-211.
Seil JT & TJ Webster, 2012. Antimicrobial applications of nanotechnology: methods and literature. International Journal of Nanomedicine 28:2767-2781.
Selvarani M, 2018. Investigation of the synergistic antibacterial action of copper nanoparticles on certain antibiotics against human pathogens. International Journal Pharmceutical Pharmacologial Science 10:83-96.
Sengupta J, S Ghosh, P Datta, A Gomes & A Gomes, 2014. Physiologically important metal nanoparticles and their toxicity. Journal of Nanoscience and Nanotechnology 14:990-1006.
Singh SP, M Kumari, SI Kumari, MF Rahman, M Mahboob & P Grover, 2013. Toxicity assessment of manganese oxide micro and nanoparticles in Wistar rats after 28 days of repeated oral exposure. Journal of Applied Toxicology 33:1165-1179.
Sloand ED & JA Vessey, 2001. Self-medication with common household medicines by young adolescents. Issues in Comprehensive Pediatric Nursing 24:57-67.
Sofowora A, E Ogunbodede & A Onayade, 2013. The role and place of medicinal plants in the strategies for disease prevention. African journal of traditional, complementary, and alternative medicines. African Journal of Traditional Complementary and Alternative Medicine 10:210-229.
Souza LMdS, M Dibo, JJP Sarmiento, AB Seabra, LP Medeiros, IM Lourenço, RKT Kobayashi & G Nakazato, 2022. Biosynthesis of selenium nanoparticles using combinations of plant extracts and their antibacterial activity. Current Research in Green and Sustainable Chemistry. 5:100-303.

Subramaniam G & M Girish, 2020. Antibiotic resistance—a cause for reemergence of infections. Indian Journal of Pediatrics 87:937–944.
Tang S & J Zheng, 2018. Antibacterial activity of silver nanoparticles: structural effects. Advanced Healthcare Material 7:1701503.
Theivasanthi T & M Alagar, 2011. Studies of copper nanoparticles effects on micro-organisms. Compound Preparation 11:1360.1372.
Thiruchelvi R, S Priyadharshini, P Mugunthan & K Rajakumari, 2022. Collagen–Zinc Oxide nanoparticles (ZnO NPs) composites for wound healing–a review. Research Journal of Pharmcy and Technology 15:2838–2844.
Tiwari PM, K Vig, VA Dennis & SR Singh, 2011. Functionalized gold nanoparticles and their biomedical applications. Nanomaterials 1:31-63.
Tuchscherer M, W Otten, E Kanitz, M Grabner, A Tuchscherer, O Bellmann & CC Metges, 2012. Effects of inadequate maternal dietary protein: carbohydrate ratios during pregnancy on offspring immunity in pigs. BMC Veterinary Research 8:1-11.
Tungmunnithum D, A Thongboonyou, A Pholboon & A Yangsabai, 2018. Flavonoids and other phenolic compounds from medicinal plants for pharmaceutical and medical aspects: An overview. Medicines 5: 109-121.
Vahdati M & TT Moghadam, 2020. Synthesis and characterization of selenium nanoparticles-lysozyme nanohybrid system with synergistic antibacterial properties. Scientific Reports 10:510.
Vandebriel RJ and WH De Jong, 2012. A review of mammalian toxicity of ZnO nanoparticles. Nanotechnology Science and Applications 20:61-71.
Von Moos N & VI Slaveykova, 2014. Oxidative stress induced by inorganic nanoparticles in bacteria and aquatic microalgae–state of the art and knowledge gaps. Nanotoxicology 8:605-630.
Xia IF, HK Kong, MMH Wu, Y Lu, KH Wong & KWHK Wo, 2022. Selenium nanoparticles (senps) immunomodulation is more than redox improvement: Serum proteomics and transcriptomic analyses. Antioxidants 11: 45-56.
Xu DP, Y Li, X Meng, T Zhou, Y Zhou, J Zheng, JJ Zhang, HB Li, 2011. Natural antioxidants in foods and medicinal plants: Extraction, assessment and resources. International Journal of Molecular Science 18:96.
Yang C, J Yang, A Lu, J Gong, Y Yang, X Lin, M Li & H Xu, 2022. Nanoparticles in ocular applications and their potential toxicity. Frontiers in Molecular Bioscience 9:203-215.
Yuan CS, EJ Bieber & BA Bauer (eds.), 2011. Traditional chinese medicine. Informa Healthcare 11:25-45.
Zinsstag J, E Schelling, D Waltner-Toews & M Tanner, 2011. From “one medicine” to “one health” and systemic approaches to health and well-being. Preventive Veterinary Medicine 101:148–156.