

ISSN: 2687-8410

DOI: 10.33552/ACCS.2025.04.000590

Archives of  
Clinical Case Studies

Iris Publishers

Review article

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# Therapeutic Potential of Silver and Cobalt Nanoparticles in Sleep Disorders, Mental Health and Diabetes

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**Received Date:** January 10, 2025

**Published Date:** January 17, 2025

## Abstract

Sleep disorders, mental health issues, and diabetes are complex and interrelated chronic conditions that significantly impact public health. Sleep disturbances exacerbate mental illnesses like anxiety and depression and impair glucose regulation, increasing the risk of diabetes. Likewise, poor glycemic control and mental health challenges contribute to disrupted sleep patterns, creating a vicious cycle. Nanomedicine, particularly the use of metallic nanoparticles such as silver (AgNPs) and cobalt (CoNPs), offers new therapeutic possibilities by enhancing drug efficacy and targeting multiple pathways simultaneously. Both AgNPs and CoNPs have demonstrated antimicrobial, anti-inflammatory, neuroprotective, and metabolic regulating properties, making them suitable for treating these interconnected conditions. This review explores the latest research on AgNPs and CoNPs in addressing sleep disorders, mental health conditions, and diabetes, while also examining the safety, toxicity, and challenges associated with their use. Finally, the paper discusses future directions for research and clinical applications, providing insights into the evolving field of nanomedicine.

**Keywords:** Circadian rhythm; disruption neuroprotection; glycemic control; oxidative stress; anti-inflammatory therapy

## Introduction

Sleep disorders, mental disorders, and diabetes are among the most important contributors to the global burden of disease. Sleep

deprivation occurs in more than one-third of the population of society and is associated with metabolic disorders, cardiovascular diseases, and psychiatric disorders [1,2]. Diabetes, for instance,



has been connected to sleep and psychiatric disorders, with up to 40% of diabetes patients being affected by insomnia or sleep disturbances [3]. value is determined by the fact that these disorders are mutually reinforcing and create a vicious cycle that reduces lifespans and overall well-being. This means that alleviating these conditions needs new therapeutic models that can impact multiple molecular signals. Nanomedicine has become an astounding discovery in the field of health care, with nanoscale materials being used beneficially in drug delivery systems. Among the transition metallic NPs, silver and cobalt NPs have emerged as potential therapeutic agents because of their multiple biological activities.

Silver nanoparticles (AgNPs) have been used for their antimicrobial, anti-inflammatory, and antioxidant properties in order to cure infection, chronic inflammation, and neurological diseases [4,5]. Cobalt nanoparticles, or CoNPs, have therapeutic applications, including enhancement of oxygen metabolism, synthesis of neurotransmitters, and glucose [6,7]. Altogether there are several possibilities of these one-and-the-same nanoparticles changing the treatment of sleep disorders, mental health disorders, or even diabetes. The investigation of the use of silver and cobalt nanoparticles in therapy is a rapidly developing area. AgNPs have been employed in health care products, including the use in medical devices, pharmaceuticals, and dressings on wounds, and CoNPs for use in metabolic balance as well as neurodegenerative diseases [8,9]. Moreover, nanotechnology has enhanced the autonomy of treatment, using nanoparticles for personalized treatment considering unique requirements of each patient.

These innovations look at how nanotechnology can be embraced in the normal provision of health care as it seeks to solve the problems arising from chronic diseases. However, the metallic nanoparticles also have some limitations, such as toxicity, biocompatibility, and effect on the environment [10,11]. AgINPs and CoNPs have been proved to induce oxidative stress, organ impairment, and bioaccumulation levels in various animals [12,13]. Current legislation regarding the usage of nanoparticles for safe and effective treatment is still under development; hence the need for more research to guide the development of standard protocols for using nanoparticles in health facilities [14]. This review synthesizes

current research findings related to silver and cobalt nanoparticles and their use in sleep, mental health, and diabetes.

## Sleep Disorders and Their Impact on Mental Health and Diabetes

Common conditions, including insomnia, sleep apnea, and restless legs syndrome, are widespread and disrupt both the physical and the emotional well-being of an individual [3]. The leading sleep disorder is insomnia that results in fatigue, cognitive impairment, and mood swings; then the probability of developing anxiety and depression rises [15]. Obstructive sleep apnea (OSA), which is defined by repeated intermittent cessation of breathing during sleep, is associated with hypertension, cardiovascular disease, and metabolic disease, with type 2 diabetes. The effects of chronic sleep loss consist in the alteration of insulin sensitivity and food intake, due to the unbalance between leptin and ghrelin, thus promoting obesity and the metabolic syndrome. Glycemic control becomes challenging when patients complain of sleep disturbances resulting from nocturnal polyuria, diabetic neuropathy, or obstructive sleep apnoea.

This is because many mental health ailments, for instance, anxiety and depression, widen sleep disorders that consequently have a detrimental impact on people's health status. This paper underlines that sleep disorders and diabetes comorbidity and their interaction with mental health processes should be treated in an integrative paradigm. Treating one condition does not necessarily mean addressing the other, but without treatment of sleep problems, mental health cannot be remedied, and glycemic control is compromised. These interconnected conditions can be addressed by nanotechnology, where there are possibilities of employing nanomaterials that can hit multiple biological targets synchronously [16]. In this regard, silver and cobalt nanoparticles are of much interest here. Due to their disputed anti-inflammatory properties, AgNPs have been employed in the devices used to treat sleep apnea to remove microbial infection and inflammation. CoNPs improve oxygen availability, which can help to ameliorate the condition of individuals with sleep apnea, as well as regulate the activity of neurotransmitters to improve mood and cognitive function (Table 1).

**Table 1:** Key Sleep Disorders and Their Impact on Mental Health and Diabetes.

Sleep Disorder	Mental Health Impact	Metabolic Impact
Insomnia	Anxiety, depression, cognitive decline	Increased insulin resistance, obesity
Sleep Apnea	Mood instability, irritability	Poor glycemic control, hypertension
Restless Syndrome	Leg Fatigue, anxiety	Cardiovascular risks, glucose dysregulation

## Role of Silver Nanoparticles in Treating Sleep Disorders, Mental Health and Diabetes

Silver nanoparticles (AgNPs) have recently benefited from a lot of considerations in nanomedicine resulting from the several therapeutic actions, which include antimicrobial, anti-inflammatory,

and antioxidant properties. In sleep medicine, AgNPs have a vital purpose of enhancing sleep quality by minimizing inflammation and microbial intrusion that affects the respiratory instruments such as the continuous positive airway pressure (CPAP) machines used to manage obstructive sleep apnoea. It was also determined that most CPAP devices are contaminated with microbial growth

that can cause respiratory infections in sleep apnea patients. It highlights the ability of the incorporation of these devices with AgNPs to enable microbial control facilitation and hygiene, thus improving uninterrupted sleep. In addition, AgNPs have crept into wearable devices, such as sleep trackers and smart garments that offer minimal skin inflammation and redness. Sleepwear textiles coated with AgNP have potential in enhancing sleep by mitigating allergic effects that hinder rest. These applications demonstrate a role for AgNPs in managing sleep hygiene as well as improving sleep quality in such chronic sleep-deprived disorders.

Besides sleep disorders, AgNPs have potential therapeutic effects on mental health disorders, of which anxiety and depression disorders are within their radar. Mood disorders involve oxidative stress and neuroinflammation; therefore, AgNPs' antioxidant capabilities reduce oxidative stress. In brain functions, AgNPs affect the concentration of serotonin and dopamine in the brain, which has to do with mood. It makes them as good subjects for future treatments of disorders like anxiety, depression, and other psychiatric ailments. Additionally, findings from animal research showed that AgNPs can help enhance learning ability and memory in addition to improving cognitive structure, giving the nanoparticles more uses in mental health treatment [17]. The use of AgNPs has several advantages in managing diabetes, as will be discussed in the following subsections. It improves insulin secretion, lessens oxidative stress, and affords relative safety to pancreatic  $\beta$ -cells at supraphysiological levels of glucose. The antibiotic property of AgNPs has also been used in the creation of dressings used in the treatment of diabetic wounds, a type of dressing that heals faster than the normal type, has lower contraction rates of infection, and promotes tissue generation [18]. Due to its ability to regulate metabolism and promote wound healing, AgNPs can be used in the management of diabetes. Currently there is evidence of the application of AgNPs in the treatment of diabetic complications, including neuropathy and diabetic foot ulcers, and the results have shown improvement in patient's symptoms.

### **Role of Cobalt Nanoparticles in Treating Sleep Disorders, Mental Health, and Diabetes**

Cobalt nanoparticles (CoNPs) are pathbreaking as they are involved in oxygen metabolism and neurotransmission and glucose control [19,20]. Such properties qualify them for the management of sleep disorders, metabolic syndromes, and mental disorders. It is crucial for CoNPs to enhance oxygen supply capabilities since sleep apnea patients would benefit from it. CoNPs increase oxygen transport in the blood; they overcome the manifestations of the obstructive sleep apnea, improving the quality of sleep and decreasing the possibilities of cardiovascular complications caused by this disorder [21]. Besides using it for sleep disorders, CoNPs revealed impressive neuroprotective activity, mainly regulating dopamine synthesis. Dopamine is one of the brain's neurotransmitters that influence mood and cognition, and low levels or high levels of dopamine have been linked to depression and neurodegenerative diseases. CoNPs facilitate the production of dopamine, which may be used in depression, anxiety, and

Parkinson's disease. First indications showed that CoNPs also keep the progression of Alzheimer's disease at bay- a condition associated with sleep disorders and cognitive impairment.

Exploring the CoNPs concept in diabetes shows that it provides important metabolic priorities. They stimulate insulin release from pancreatic  $\beta$ -cells, increase glucose utilization, and decrease oxidative stress, thus glycemic control. For instance, Cinnamon CoNPs given orally have been found to prevent or control diabetes because they alleviate insulin resistance in experimental type 2 diabetic animals. Concurrently, CoNPs have been incorporated into advanced wound dressing platforms for patients with diabetes that induce vasculogenesis and tissue repair, thereby protecting the patient from opportunistic infections and amputations. Because of these multiple functions, CoNPs may become the basis for future therapies for diabetes and its complications. Nevertheless, risks are signified when employing CoNPs, which are discussed in the subsequent section. Cobalt has been reported to cause oxyradical stress, organ injury, and hematology change when administered in high doses, and thus there is a potential inconsistency safety issue about the CoNPs if continuously consumed by people in the long-term future. Request to reduce these risks; attempts are being made towards getting the right size, coating, and dosing of CoNPs to enable safe application in clinical practice.

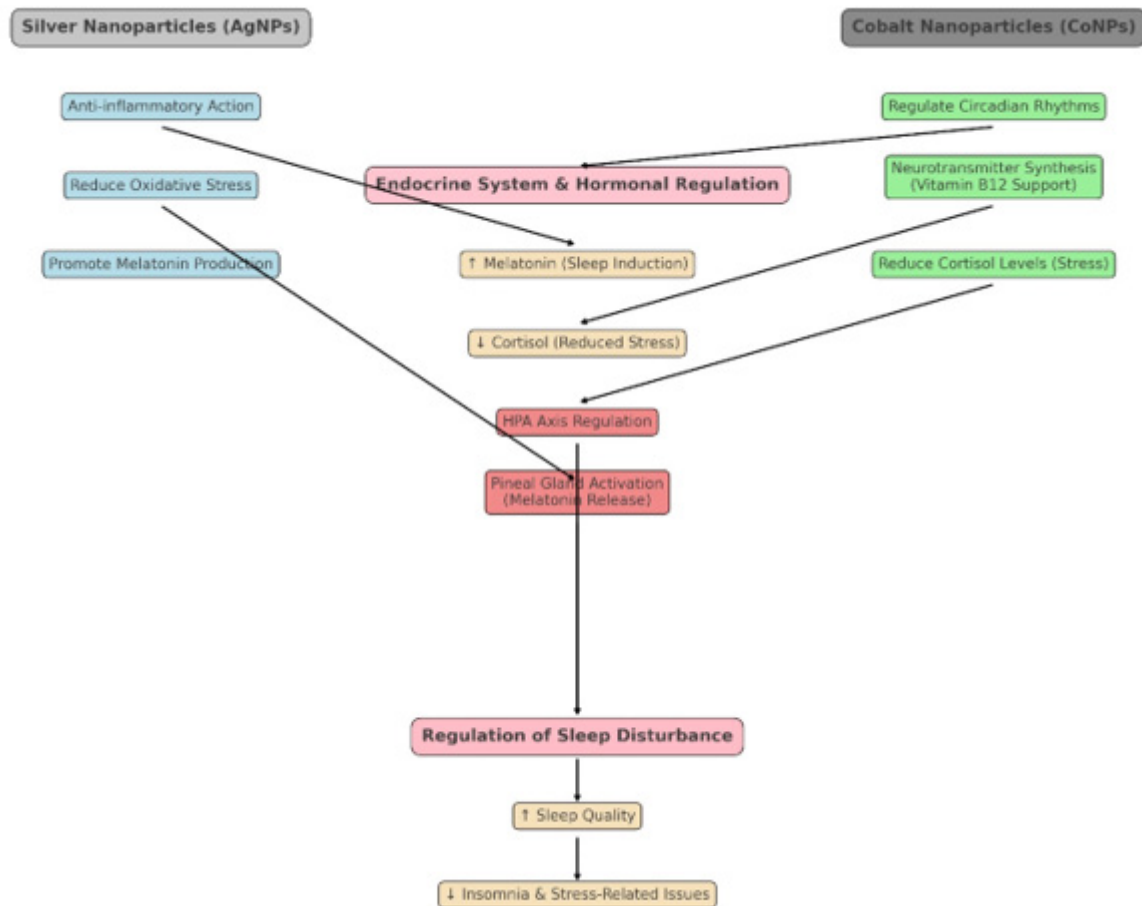
### **Mechanism for the Management of Sleep**

The figure depicts how AgNPs and CoNPs cause sleep disruptions by forbidding endocrine and hormonal controls. The pathophysiological roles of AgNPs include inflammation inhibition and oxidative stress, which boost melatonin synthesis, a hormone that controls sleep. Higher levels of melatonin promote sleep and also regulate one's biological clock, whereas lower stress hormone cortisol also contributes positively to sleep quality [22]. On the other hand, CoNPs have their roles observed by modulating circadian rhythm and synthesis of neurotransmitter through the Vitamin B12 pathway for mood swing balance and allayed stress. Synergistically, both AgNPs and CoNPs act on the hypothalamic-pituitary adrenal (HPA) axis, which is involved in cortisol regulation, decreasing stress and providing relaxation. Also, gating opens the pineal gland to release melatonin, which strengthens sleep wakefulness cycles and thus sleeping. Thus, these nanoparticles improve sleep quality and decrease the level of insomnia and stress-related issues that could be used for the therapy of sleep disorders.

Such an integrated concept summarizes the interaction between oxidative stress, hormone level, and circadian rhythm, explaining how these suppressive nanoparticles affect the functioning of AgNPs and CoNPs to enhance global mental health and sleep cycle (Figure 1). A flowchart is used herein to depict how the respective pathways of AgNPs and CoNPs influence mental health through the endocrine system and hormonal balance. Therefore, it has been understood that AgNPs offered anti-inflammatory activity and antioxidant properties as well, which are responsible for neuro prolongation through the prevention of cell death in the brain. Such actions increase the secretion of serotonin-a hormone that modulates the mood in the body. In like manner, CoNPs help to maintain positive

mental health by synching the biological clock and participating in neurotransmitter production via Vitamin B12 biosynthesis. These nano constructs augment the synthesis of melatonin to regulate

sleep and decrease stress through lowering cortisol concentrations. These changes in hormones are controlled through the HPA axis, and the stress system is essential to regulating stress.

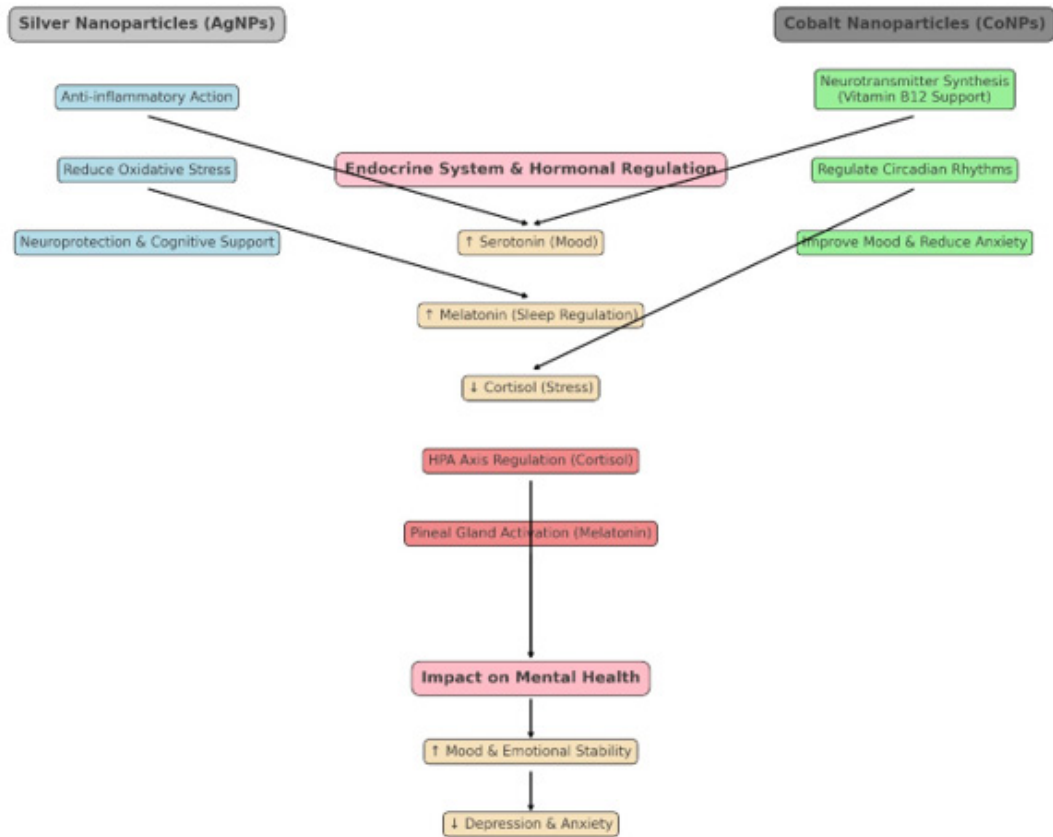


**Figure 1:** Mechanism of Sleep Disturbance Regulation via Silver (AgNPs) and Cobalt Nanoparticles (CoNPs).

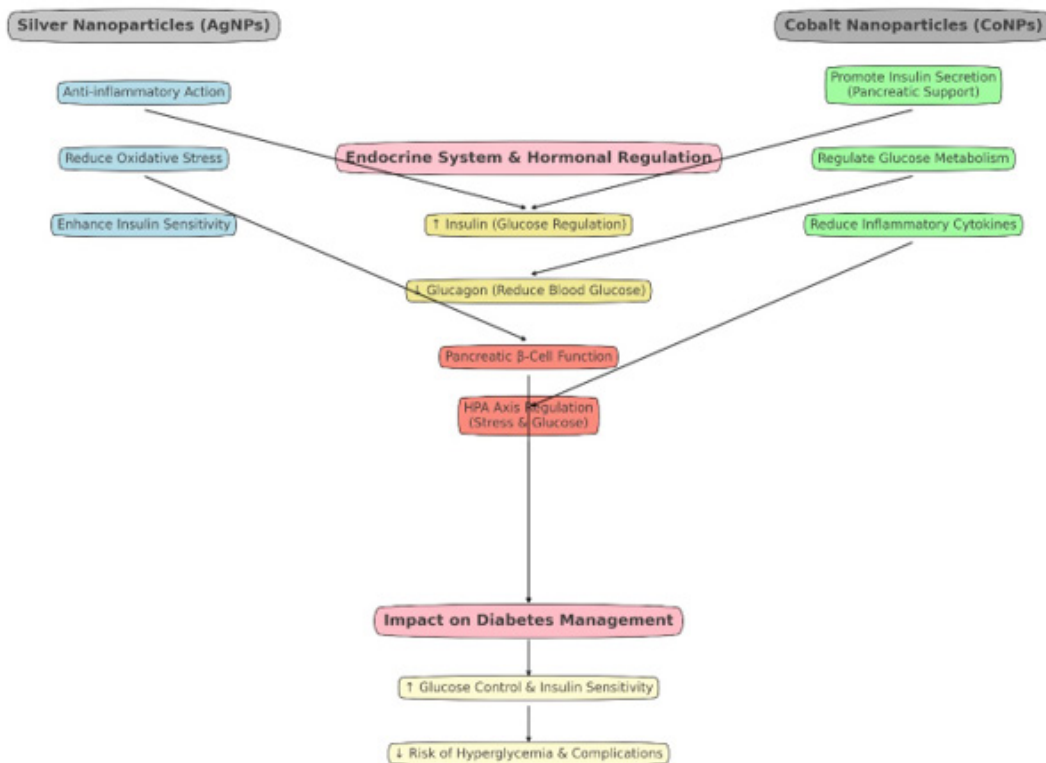
As an added benefit, the stimulation of the pineal gland makes sure that there is enough of the sleep-regulating hormone-melatonin-in the body, thus balancing the sleep-wake cycle. Altogether, these nanoparticles have a strong influence on improving mental well-being, increasing mood, and decreasing all factors related to depression and anxiety. Altogether, the modulatory effects on neurotransmitter homeostasis, stress, and sleep contributions of AgNPs and CoNPs show their efficacy in the enhancement of cognitive ability and mood regulation (Figure 2). It also shows the way silver nanoparticles (AgNPs) and cobalt nanoparticles (CoNPs) help in enhancing diabetes control through endocrinology and metabolism. Anti-inflammatory properties and attenuation of oxidative stress were observed by AgNPs, improving insulin signalling and preserving pancreatic  $\beta$ -cells for insular insulin release. At the same time, CoNPs enhance insulin release for their ability to diminish  $\beta$ -cell dysfunction and manage glucose

homeostasis, eliminating the possibility of hyperglycaemia.

The nanoparticles also act hermetically—AgNPs upregulate glucose metabolism, and CoNPs decrease glucagon concentrations, effectively normalising blood glucose. In addition, both nanoparticles affect the stress heptapeptide axis and play a role in regulating glucose levels based on cortisol secretion. This double protection is not only safeguarding metabolic homeostasis but also maintaining the functionality of the endocrine  $\beta$ -cells, significant for the management of T2DM. Combinedly, the studied AgNPs and CoNPs stimulate glucodynamics and enhance insulin utilisation, leading to a lower propensity of hyperglycaemia and its consequences such as neuropathy and cardiovascular disease. This integrated approach underscores the idea of these nanoparticles, COX-2i and INS-RED, for therapeutics in diabetes by targeting these three aspects through reduction of oxidative stress, regulation of hormones, and enhanced glucose metabolism (Figure 3).



**Figure 2:** Mechanisms of Mental Health Regulation through Silver (AgNPs) and Cobalt Nanoparticles (CoNPs).



**Figure 3:** Mechanism of diabetes Regulation via Silver (AgNPs) and Cobalt Nanoparticles (CoNPs).

## Safety, Toxicity, and Challenges of Using Silver and Cobalt Nanoparticles

Among these nanoparticles, silver (AgNPs) and cobalt nanoparticles (CoNPs) have tremendous therapeutic applications with safe usage in clinics only if biocompatibility is maintained. Biocompatibility stands for the compatibility of these nanoparticles with biological systems and the negative impact on biological systems. Previous studies have shown that both AgNPs and CoNPs are biocompatible in a dose-dependent manner, with controlled doses exhibiting positive cell and tissue interaction. Nevertheless, at higher concentrations or with long-term exposure, these nanoparticles could alter normal biological functioning, thus the need to closely monitor and adjust their dispersion formulations to minimise toxicity impacts. Altering the surface of nanoparticles, for example, through polymeric or functionalisation, has enhanced biocompatibility, reduced immunogenicity, and enhanced nanoparticle stability in biological media. This is one of the restrictive factors that hold the therapeutic value of the drugs in check due to the proven toxicity effects that are strongly associated with long-term usage of the drugs.

The research indicates that AgNPs possess the ability to bioaccumulate and cause toxicity and generate metabolic stress and morphological changes in the hepatic, renal, and cerebral organs, respectively. Likewise, CoNPs may cause variation in

peripheral blood count and oxidative stress that may affect the heart, lungs, and blood cells. Besides, the toxic effects of organ A549, both nanoparticles have the ability to affect the antioxidant ability, thereby increasing the level of oxidative stress and cellular dysfunctions. These effects can be reduced, and nanoparticles protected from interactions with healthy tissues that may be dangerous, through the creation of biocompatible coatings and by encapsulation of the nanoparticles within nanocarrier systems. Pollution is another difficulty, as metallic nanoparticles reach out for the biosphere and penetrate the food web and alter microbial consortia. To tackle such issues, the researchers are working on effective green synthesis of nanoparticles by using plant extracts and eco-friendly chemicals.

Regulatory agencies have also stepped up to developing monitoring structures through which nanomaterials can be released and used in the health and industrial sectors sustainably (Table 2). As far as safety increases are concerned, further long-term research should be conducted to evaluate the safety of these nanoparticles. According to the FDA, ECHA under REACH, and OECD, extensive toxicological studies are required before nanoparticles can be used in the treatment of any disease. Future studies should thus strive to improve nanoparticle formulations to reduce likely adverse effects while at the same time making gains in the likely benefits of the nanoparticles.

**Table 2:** Biocompatibility and Toxicity of Silver and Cobalt Nanoparticles.

Nanoparticle	Property	Toxicity Concern	Affected Organ/Function	Biocompatibility Solution	Reference
Silver (AgNPs)	Antimicrobial	Oxidative stress	Liver	Polymer coating to reduce toxicity	Khan et al. (2022)
Silver (AgNPs)	Anti-inflammatory	Nephrotoxicity	Kidneys	Encapsulation in lipid nanocarriers	Hosseini et al. (2024)
Silver (AgNPs)	Antioxidant	Neurotoxicity	Brain	Surface modification with biopolymers	Sharma et al. (2015)
Silver (AgNPs)	Antiviral	Mitochondria l dysfunction	Heart	Dosing adjustments	Malik et al. (2023)
Cobalt (CoNPs)	Oxygen regulation	Morphologic al alterations	Lungs	Controlled release systems	Umar et al. (2024)
Cobalt (CoNPs)	Neurotransmitter modulation	Oxidative stress	Brain	Nano-lipid carriers for brain targeting	Behera et al. (2023)
Cobalt (CoNPs)	Angiogenic	Hematologic al toxicity	Blood	Surface engineering for stability	Mandakhba yar et al. (2024)
Cobalt (CoNPs)	Antidiabetic	Cardiovascular risks	Heart	Combination with antioxidants	Sharda & Choudhury (2023)
Both	Drug delivery enhancer	Bioaccumulation	Multiple organs	Green to synthesis minimize toxicity	Sivalingam et al. (2024)
Both	Nanocarrier potential	Disruption of antioxidant activity	Cells	Tailored surface functionalization	Paul et al. (2024)

## Ethical Guidelines and Safety Measures for the use of Nanoparticles in Medicine and Healthcare

### Compliance with International Ethical Standards

Nanoparticles (NPs) in healthcare should do this considering the global ethical principles such as the Declaration of Helsinki that acknowledges that wellbeing and protection of human participants engaged in research should always trump the risk factors [23]. This entails conducting NP-based clinical trials with adequate Chemical and Biological Standard Operating Procedures relative to participant protection especially in developing new NP treatment. The participants also need to follow Good Clinical Practice (GCP) standards as they react to boosting the trial's concordance with scientific correctness, the safety of the participants, and the general ethicality of the clinical trial phases.

### The Information that must be Disclosed will be the Subject of Informed Consent

Anyone entering trials or treatments employing NP-based interventions should be provided adequate and extensive details of the gains, dangers, and likelihoods inherent in the technologies. This has applicability in averting forced participation to ensure that all individuals participating in a certain study, experiment or trial have chosen to take part willingly [24]. Particular focus should be paid to mitigation of risks of treatments with new generation applied nanotechnologies, emphasizing the experimental character of such treatments.

### Rules for Assertion of Safety and Toxicity

In line with the FDA and EMA guidelines, the manufacturers of nanoparticles intended for use in healthcare delivery have to undergo laboratory testing across toxicity and biocompatibility. : These assessments are done with an emphasis on toxic effects at increasing exposure levels, accumulation and chronic toxicity, and cytotoxicity [25]. Major organs should be evaluated to assess the nanoparticles' outcome, particularly if they can penetrate the biological barriers, including the blood-brain barrier.

### Environmental and Waste Management Guidelines

The positive effects of nanoparticles in reductions of environmental contamination risks are applied in healthcare systems and research beneath the regular sustainable waste management practices. Disposal of NP-based materials has been considered unsafe for the environment and in wildlife and human consumption, bioaccumulation has been cited by Summer and others (2024). Consequently, it is imperative that those of environmental protection are incorporated in the health care for adequacy in the management of nanomedical waste.

### Precautionary Principle and Risk Benefit Analysis

The precautionary principle proposed that no matter how favourable the benefits are, nanoparticle-based treatment must only be adopted where risks are properly understood and are commensurate to the expected outcomes. This implies that the clinical practice guidelines of NPs have to remain constantly revised

as more information on the safety and efficacy of NPs is generated.

### Board Complicity & Ethical Committees

IRBs and ethical overseeing committees are important for supervising nanomaterial research owing to conformity to ethical concepts and patients' wellbeing [26]. These committees ensure that the threats posed by nanoparticle-based treatments are tolerable compared to the perceived benefits by society. It also provides iterative checking of compliance to regulations in the course of trials and in post-market evaluation.

### Models of Chronic Disease Management and Patient-centred Care

Nanoparticles are becoming important input for developing the outlook for a personalized medical system where treatments are adjusted to specific patient's requirements. Nonetheless, care providers need to make nanoparticle treatments affordable to all and it is the role of policy makers to ensure that benefits of technology do not limit access to care. Ethical norms should protect the society against poor use of the nanotechnology that is adopted widely in the society.

### Current Research and Future Directions

Recent literature reviews on silver and cobalt nanoparticles show their efficacy in dealing with chronic diseases and diseases: sleep disorders, mental health disorders, and diabetes. It's currently in clinical trials to determine the benefit of these nanoparticles as a sleep regulator, a neurotransmitter balancer, as well as an insulin sensitizer. Here, the administrative potential of AgNPs and CoNPs, which are non-specific in their therapeutic action, is explained by their ability to treat multifactorial and mutually connected diseases. For instance, AgNPs used in diabetic wound care are effective not only in wound healing but also in preventing infection, giving a two-in-one solution [27]. Likewise, CoNPs increase oxygen diffusion, which may help treat obstructive sleep apnoea at the same time the nanoparticles contribute to dopamine production for mental health enhancement. Other advanced nanocarrier systems have gone further to enhance the therapeutic efficacies of these nanoparticles through controlled delivery. Scientists have proposed opportunistic nanomedicine in which drugs depend on the genetic and metabolic makeup of the patient.

These anticipations are specifically motivating for diabetes treatment, in which CoNPs can boost insulin discharge and AgNPs can improve the function of  $\beta$ -cells and the signal recognition of oxidative stress. However, the following problems persist: more research on safety is needed to establish the long-term effect on human beings due to extended use of these nanomaterials. However, it's worth accepting that they are relatively expensive and there are no unified rules on how they should be produced [28]. Only through cooperation with other healthcare professionals, researchers, and with the help of government regulating bodies, will it be possible to deal with the above-mentioned barriers and safely introduce nanoparticles into the wide range of interrelated medical practices. In the future, the synthesis of more effective formulations, in which AgNPs and CoNPs are combined with traditional treatments that

target multiple diseases, would improve the quality of life for people with a chronic illness. Future studies should also begin to examine eco-friendly synthesis methods in order to reduce the amount of harm done to the environment relative to nanoparticle preparation. New breakthroughs in the use of artificial intelligence in drug development and nanorobotics may extend the field's existing possibilities by exploring ways to address other intricate diseases.

## Conclusion

It has been evidenced that silver and cobalt nanoparticles have the highest prospects in treating sleep disorders and other mental disorders, including diabetes. These nanoparticles have attracted much attention in the medico-pharmaceutical field due to their antibacterial, anti-inflammatory, and neuroprotective properties. Overall, sleep quality has been improved by AgNPs, particularly on wound healing as well as reducing the level of oxidative stress. Conversely, CoNPs have the potential of exerting action on neurotransmitters, angiogenesis, and secretion of insulin. In combination, these nanoparticles employ an integrated system approach to address often comorbid chronic diseases. However, some concerns on the issues inclusive of safety, toxicity, and environmental aspects have to be met before these nanoparticles might be more incorporated into clinical practice. This makes continuous research necessary to fine-tune their composition, make enhancements on their compatibility, and put in place measures to ensure that there is safe usage. Enhancements in nanomedicine and products for nanotheranostics, targeted therapies, and Cobo metabolic therapies should also provide enhanced patient benefit. Even further advancement, solid cooperation of silver and cobalt nanoparticles can turn into an excellent tool aimed at the improvement of the quality of life for millions of patients with chronic diseases.

## Acknowledgement

None.

## Conflict of Interest

All authors have no conflict of interest.

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