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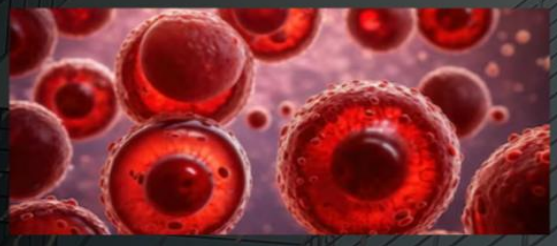

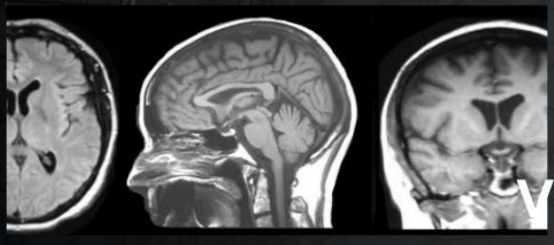

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Aims & Scope

The Journal aims to publish research in all fields of clinical, diagnostic, experimental & preventive areas related to medical sciences to disseminate scholastic work among clinicians and scientists around the globe.

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Editorial

CHILDHOOD EXPOSURES AND DEFICIENCIES AS DETERMINANTS OF CANCER RISK IN ADULTHOOD

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ABSTRACT:

Cancer development is increasingly recognized as a life-course process influenced by early-life exposures and nutritional status. During critical periods of growth and development particularly first 1000 days, biological systems are particularly susceptible to carcinogenic insults and epigenetic modifications that may predispose individuals to malignancy later in life. Deficiencies in key nutrients such as folate and vitamin D can impair DNA repair and immune function, while early exposure to environmental toxins and pollutants contributes to genomic instability and endocrine disruption. Additionally, persistent infections—including Hepatitis B (HBV), Human papillomavirus (HPV), and Helicobacter pylori infection—play a significant role in infection-related cancers, particularly in low- and middle-income countries. Socioeconomic disparities further exacerbate these risks by limiting access to nutrition, healthcare, and preventive interventions. Addressing these early determinants through integrated public health strategies—such as improved childhood nutrition, vaccination programs, and environmental regulation—offers a critical opportunity for cancer prevention. A shift toward early-life interventions is essential to reduce the long-term global cancer burden and advance equitable health outcomes.

Keywords: Early life exposures, life time cancer risk, environmental exposures, nutritional deficiencies

INTRODUCTION

Cancer is increasingly understood not merely as a disease of aging but as the cumulative outcome of life-course exposures, many of which originate in early development particularly first 1000 days of life. The paradigm linking early-life environment to adult disease—central to the Developmental Origins of Health and Disease (DOHaD) framework—has profound implications for oncology. Childhood represents a critical window of biological vulnerability during which environmental insults, nutritional deficiencies, and epigenetic modifications can predispose individuals to malignancy decades later.

Early age biological programming of cancer risk

Rapid cellular proliferation, organogenesis, and immune system maturation characterize childhood. During this period, exposure to carcinogens or deprivation of essential nutrients can induce long-lasting molecular alterations. Epigenetic reprogramming—through DNA methylation, histone modification, and microRNA expression—can dysregulate oncogenes and tumor suppressor genes without altering DNA sequence. These early changes may remain latent until triggered by additional exposures later in life, resulting in carcinogenesis. Moreover, immune surveillance mechanisms, which play a critical role in eliminating malignant cells, are shaped early in life. Nutritional deficiencies or chronic infections during childhood may impair immune competence, reducing the body's ability to prevent tumor initiation and progression. Childhood exposures are deeply embedded in socioeconomic context. Poverty influences nutrition, environmental safety, access to healthcare, and education—all of which modulate long-term cancer risk. Children growing up in disadvantaged settings are more likely to experience cumulative risk exposures, creating a trajectory of vulnerability that extends into adulthood.

Childhood nutritional deficiencies and cancer susceptibility

Malnutrition remains a persistent challenge in low- and middle-income countries (LMICs), including Pakistan. Deficiencies in micronutrients such as vitamins A, D, folate, and zinc have been implicated in increasing cancer susceptibility. Folate deficiency disrupts DNA synthesis and repair, increasing the likelihood of mutations. Vitamin D deficiency has been associated with higher risks of colorectal, breast, and prostate cancers due to its role in cell differentiation and apoptosis. Antioxidant deficiencies (vitamins C and E) reduce the capacity to neutralize oxidative stress, facilitating DNA damage. Chronic undernutrition may also lead to growth inhibition, which has

been linked with metabolic dysregulation and increased risk of certain adult malignancies. Thus, nutritional status specially micro-nutrients in childhood must be carefully watched and any malnutrition must be treated as the top priority.

Environmental and Chemical Exposures

Children in many regions are disproportionately exposed to environmental carcinogens including air pollution (particulate matter, polycyclic aromatic hydrocarbons), pesticides and agricultural chemicals, heavy metals such as arsenic and lead in drinking water and second-hand tobacco smoke. These exposures can induce DNA damage, oxidative stress, and endocrine disruption. For example, early exposure to endocrine-disrupting chemicals may alter hormonal pathways, increasing the risk of hormone-dependent cancers such as breast and prostate cancer in adulthood. In situations where there is high exposure of carcinogens and there is micronutrients deficiency and there is not enough anti-oxidants to neutralize oxidative stress and lack of vitamin to help in DNA repair the risk of cancer increases many folds.

Infectious Agents and Chronic Inflammation

Childhood infections are another critical yet under-recognized contributor to adult cancer risk. Persistent infections can lead to chronic inflammation and oncogenic transformation. Notable examples include: Hepatitis B and Hepatitis C infections acquired early in life, predisposing to hepatocellular carcinoma, Human papillomavirus, associated with cervical and other anogenital cancers, Helicobacter pylori infection, linked to gastric cancer, Epstein Bar virus to lymphoma. In LMICs, where vaccination and early treatment coverage may be suboptimal, the burden of infection-related cancers is particularly high.

Implications for Prevention and Policy

Recognizing cancer as a life-course disease necessitates a shift from reactive to preventive oncology. Interventions must begin early, especially considering first 1000 days of life:

1. Strengthening maternal and child nutrition programs
2. Expanding vaccination coverage (e.g., HBV, HPV)
3. Reducing environmental exposures through regulatory enforcement
4. Improving water, sanitation, and air quality
5. Integrating early-life risk awareness into public health strategies

Institutions such as World Health Organization have emphasized the importance of early prevention, yet implementation gaps remain substantial in many LMICs.

Research and Future Directions

There is a pressing need for longitudinal cohort studies in diverse populations to better quantify the relationship between childhood exposures and adult cancer outcomes. Biomarker discovery, epigenetic profiling, and life-course epidemiology should be prioritized to identify high-risk groups and inform targeted interventions. Academic institutions, particularly in LMICs, have a critical role to play in generating context-specific evidence and translating it into policy.

CONCLUSION

The development of cancer is a course of decades, establishing body environment suitable for cell proliferation requires multiple factors including weak immune system to kill cancer cells resulting from long term micronutrient deficiency, lack of anti-oxidant supply to balance oxidative stress. Addressing childhood exposures and deficiencies offers a strategic opportunity to reduce the global cancer burden. Thus shifting strategies from treatment prevention would be pragmatic approach.

Conflict of Interest

Author declare no conflict of interest.

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Original Article

COLOR VISION DEFECT IN PHAKIC VERSUS PSEUDOPHAKIC EYE GROUP

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ABSTRACT:

This study was aimed to determine the color vision defect in pseudophakic and phakic groups.This was a cross-sectional study with non-probability convenience sampling. The patients' age ranged between 45 and 60 years, and they had a follow-up after one month of surgery. The visual acuity recorded ranged from 6/6 to 6/18 after refraction. All types of refractive errors after phacoemulsification surgery (acrylic IOL) were included. Posterior subcapsular opacity and other types of cataract surgery were excluded. The Panel D-15 test was used to assess color vision defects. Ethical approval was obtained from the institutional Research Ethical Committee (REC). Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 20.0.A total of 160 eyes were enrolled in this study. Among these, 70 (44%) and 90 (56%) eyes belonged to males and females, respectively. The eyes were categorized into two groups: 80 (50%) were phakic and 80 (50%) were pseudophakic. Among the 80 pseudophakic eyes, 32 eyes had tritanopia (40%), 10 eyes had deuteranopia (13%), 8 eyes had protanopia (10%), 6 eyes had combined tritanopia and protanopia (8%), 4 eyes had combined deuteranopia and tritanopia (5%), 2 eyes had protanopia and deuteranopia (3%), and 18 (23%) had no defect. Among the 80 phakic eyes, 72 (90%) had no defect, while deuteranopia was found in 1 (1.25%) eye and tritanopia in 7 (9%) eyes. Tritanopia was most commonly observed in the pseudophakic group, while the majority of the phakic group did not show any color vision defect.

Keywords: Pseudophakic, Phakic, Panel d-15, acrylic (IOL), color vision defects

INTRODUCTION

Color vision is a feature of perception that is the ability to perceive differences between lights composed of different wavelengths, independently of light intensity. There are three kinds of color-vision genes in humans: a "blue" pigment gene on chromosome 7, and "red" and "green" pigment genes located at the tip of the long arm of the X chromosome-Xq28 (1). The corresponding pigments are located in three different classes of retinal cone cells, each containing a different photo pigment. These pigments have characteristic maximal absorption spectra: 420 nm or shortwave (blue), 530 nm or middle wave (green), and 560 nm or long wave (red) (2). Color vision perception can be classified into three types based on wavelength sensitivity: Monochromats, Dichromats, and Anomalous Trichromats.

Mechanism of color vision: The eye forms images based on differences in the reflectance of light from external objects. Small perturbations, in contrast, are processed through a center-surround system, where surrounding background luminance is subtracted from the center signal, highlighting the local features of the central signal (3). This system provides high sensitivity to light-dark contrast (4).

Color vision deficiencies diminish the capacity to distinguish certain colors under specific circumstances and its testing identify the existence, type, and severity of defects, providing a basis for the evaluation of the defect's impact on personal and professional performance (5). Color vision discrimination deteriorates with progressing age (6). Ocular diseases such as cataract and glaucoma, trauma, and certain medications also affect color vision (7). Chromatic discrimination is assessed using various color vision tests (8-9).

In European Caucasians the prevalence of color vision deficiency is about 8% in men and about 0.4% in women and between 4% and 6.5% in men of Chinese and Japanese ethnicity, respectively (10). Some regional prevalence studies showed diversity in prevalence such as Turkey (7.3%), Iran (4.7%), India (2.8% to 8.2%, ethnic variations) and Saudi Arabia (2.9%) (11). While in Pakistan, color vision deficiency (CVD) ranges from 0.9% , 2.48% and 2.78% (12-14).

METHODS

This cross-sectional study with non-probability convenience sampling was carried out in the Department of Ophthalmology and Visual Science, Dow University of Health Science and Isra School of Optometry, Al-Ibrahim eye hospital, Karachi, Pakistan. Both male and female patients were included. The protocol for examination for all patients who met our inclusion exclusion criteria were filled. Visual acuity was recorded separately both for near and distance vision, with and without glasses and with pinhole. A total of 160 eyes were enrolled with 80 eyes pseudophakic and 80 eyes phakic. The patients aged between 45 years to 60 years old havinf Phacoemulsification surgery with Acrylic IOL implant, came for follow-up after one month were included. All types of refractive errors after cataract extraction and visual acuity ranges from 6/6 to 6/18 were included. Posterior sub capsular opacity and other types of cataract surgeries and systemic diseases were excluded. Panel D15 test was performed at 33cm distance to find the changes in color vision. Self-prepared proforma was used for collection of data.

Statistical methods

Statistical analysis was performed using statistical package for social science (SPSS) version 20.0. All the categorical variables were presented as frequencies and percentages.

RESULTS

The eyes were categorized in two groups: Phakic group with 80 (50%) eyes and pseudophakic group with 80(50%) eyes in a total sample of 160 eyes. All included sample was examined for right and left eye separately. Among them 86 (54%) were right eyes and 74 (46%) were left eyes. The visual acuity both in pseudophakic and phakic, 6/18 were in 5 (6%) pseudophakic eyes, 6/12 in 8 (10%), 6/9 in 32 (40%) and 6/6 in 3 (44%) eyes. But in phakic, 6/18 were 3 (4%), 6/12 in 5 (6%), 6/9 in 14 (18%) and 6/6 in 58 (73%) eyes as shown in Table 1.

Table 1. Distance visual acuity

Visual acuity	Groups				Total Eyes
	pseudophakic	Percentage%	Phakic	Percentage%	
6/18	5	(6%)	3	(4%)	8
6/12	8	(10%)	5	(6%)	13
6/9	32	(40%)	14	(18%)	46
6/6	3	(44%)	58	(73%)	93
Total	80	(100%)	80	(100%)	160

The near vision in both groups pseudophakic and phakic;N6 in 45 (52%) pseudophakic eyes and N8 in 35(47%) pseudophakic eyes, but in phakic 41 (48%) eyes with N6and 39 (53%) eyes with N8 as shown in Table 2.

Table 2. Near visual acuity

Group	Near Vision				Total Eyes
	N6	Percentage%	N8	Percentage%	
pseudophakic	45	52%	35	47 %	80
Phakic	41	48 %	39	53 %	80
Total	86	100 %	74	100 %	160

In Pseudophakic group myopes were 15 (19%), hyper metropes 12 (15%), astigmatic 32 (40%) and 21 (26%) had no refractive error. In phakic group myopes were 12 (15%), hypermetropes 7 (9%), astigmatic 17 (21%) and 44 (55%) had no refractive error as shown in Figure 1. Among pseudophakic group; tritonopia in 32 (40%), deutronopia in 10 (13%), protonopia in 8 (10%), combined tritonopia+protonopiain6(8%),combineddeutran+tritan in 4 (5%), combined protan + deutran in 2 (3%) eyes while 18 (23%) eyes showed no color vision defect as shown in Figure 2.

The color vision defect in Pseudophakic Group when compared with Phakic Group (Figure 4), the pseudophakic eyes were more sensitive to tritanopia 32 (40%) as compared to phakic 7 (9%), than deutronopia 10 (13%) in pseudophakic group and only 1(9%) in phakic group, protonopia 8(10%)in pseudophakic and 0 (zero) in phakic and the combined tritonopia+protonopia defect 6 (8%) in pseudophakic but 0 (zero) in phakic, then combined deutronopia + tritonopia 4 (5%) in pseudophakic and 0 (zero) in phakic group, combined protonopia +deutronopia 2 (3%) in pseudophakic and 0 (zero) in phakic while 18 (23%) in pseudophakic and 72 (90%) in phakic group has no color vision defect.

Figure 1: Type of refractive errors in Pseudophakic and phakic groups

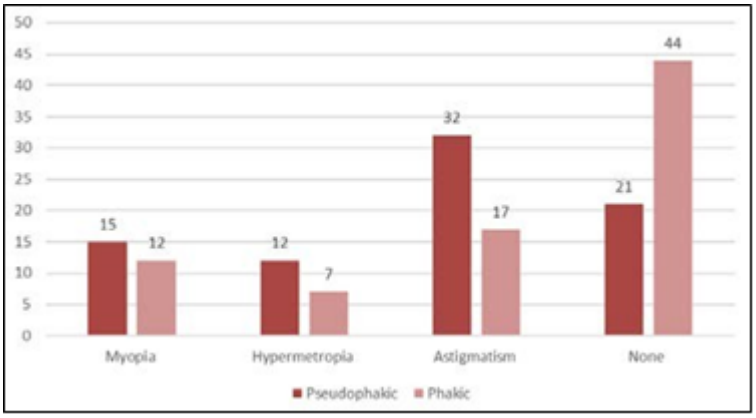
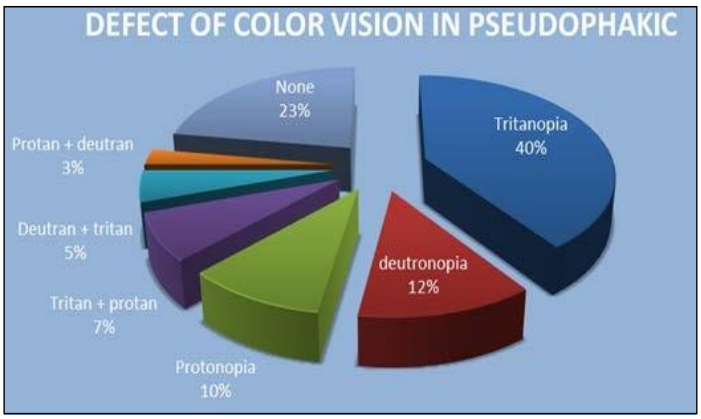


Figure 2: Defect of color vision in Pseudophakic Group



In phakic group: Tritonopia in 7 (9%) eyes and Deutronopia 1(1.00%) while 72 (90%) had no defect as shown in Figure 3.

Figure 3: Defect of color vision in phakic Group

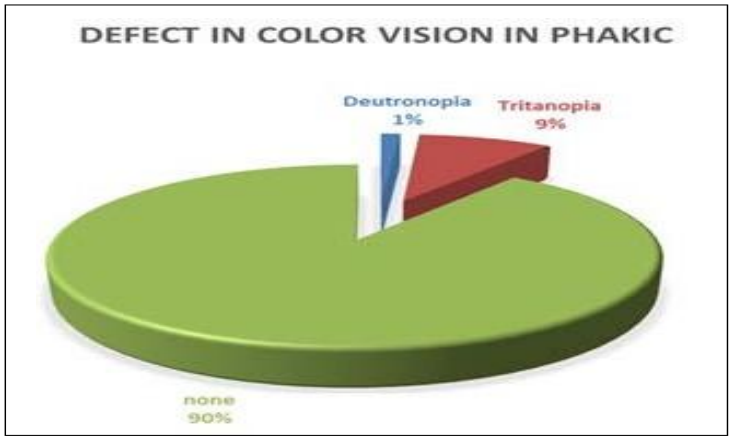
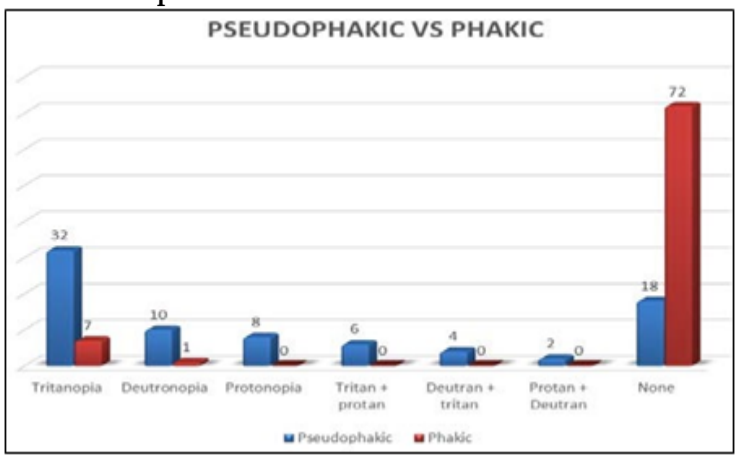


Figure 4: Color vision defect in Pseudophakic Group vs Phakic Group



DISCUSSION

In the present study Pseudophakic group was more sensitive to tritonopia which contradict with the results of another study where anomaloscope and the 100-hue test were used indicating that the pseudophakic eyes were more sensitive to red and less sensitive to blue than healthy phakic eyes (15).

A study conducted on sixty-eight eyes of 40 diabetic patients, divided into four subgroups based on different stages of diabetic retinopathy, and 20 eyes of 10 healthy controls, demonstrated that only 51% of diabetic patients passed the Ishihara pseudoisochromatic plates test, 28% failed, and 21% were classified as suspects, whereas 90% of controls passed and 10% failed. In the Farnsworth D-15 test, only 10% of controls failed, due to protanopia, while 50% of diabetic patients showed test failure, exhibiting various forms of dyschromatopsia, predominantly tritanopia and combined color vision deficiencies. These findings contrast with our study, which excluded participants with systemic diseases (16).

Another cross-sectional study used the Farnsworth 100 hue test and Pickford-Nicholson anomaloscope in pseudophakic, phakic, and spectacle aphakic eyes to determine the minimal difference in their color perception. The pseudophakic eyes were highly sensitive to red and less sensitive to blue when compared with aphakic eyes, while in our study, Panel D15 was used to assess color vision defects and showed contrary results, indicating that pseudophakic eyes were sensitive to blue(17). A study showed that blue-yellow defects became increasingly prevalent with increasing age (18) similar to our study's results.

Another study compared color differentiation of 30 phakic and 30 pseudophakic eyes using the Farnsworth-Munsell 100-hue test, and they found no significant difference between the two groups regarding color differentiation, although theoretically it could be expected that color differentiation would be better in eyes with a synthetic

intraocular lens and depending on the subject's age (19). It has the greatest influence on color sense, while our study showed that the pseudophakic group is more sensitive to blue defects compared to the phakic group.

CONCLUSION

The study concluded that tritanopia was more commonly present in Pseudophakic group while majority of subjects in Phakic group did not show color vision defect.

Conflict of Interest

Authors declare no conflict of interest.

Ethical consideration

The study was approved by local research ethics committee.

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Original Article

SYNTHESIS OF *TAVERNIERA NUMMULARIA*-MEDIATED SILVER NANOPARTICLES FOR ENHANCED ANTIMICROBIAL AND ANTIOXIDANT ACTIVITIES

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ABSTRACT:

This study was designed to synthesize silver nanoparticles (AgNPs) using Taverniera nummularia leaf extract through a green synthesis approach and to evaluate their antimicrobial and antioxidant activities. Silver nanoparticles were synthesized using aqueous extracts of Taverniera nummularia leaves as a reducing and stabilizing agent. Characterization of the synthesized nanoparticles was carried out using UV–visible spectroscopy, Fourier Transform Infrared Spectroscopy (FTIR), Scanning Electron Microscopy (SEM), and X-ray Diffraction (XRD). Antibacterial activity was evaluated against Klebsiella pneumoniae, Escherichia coli, and Staphylococcus aureus. Antioxidant activity was assessed using DPPH, ABTS, and hydrogen peroxide scavenging assays. The UV–visible spectrum showed a characteristic surface plasmon resonance peak at 407 nm, confirming the formation of AgNPs. FTIR analysis revealed hydroxyl functional groups from plant biomolecules responsible for the reduction of silver ions. SEM analysis confirmed spherical nanoparticles with sizes ranging from 120–200 nm. XRD patterns demonstrated the crystalline structure of the synthesized nanoparticles. The green synthesized AgNPs exhibited antibacterial activity against the tested bacterial species. Additionally, significant free radical scavenging activity was observed in DPPH, ABTS, and hydrogen peroxide assays, indicating notable antioxidant potential. Taverniera nummularia leaf extract is an effective reducing and stabilizing agent for the green synthesis of silver nanoparticles. The synthesized AgNPs demonstrate promising antimicrobial and antioxidant properties and may have potential applications in biomedical research, particularly in the development of nano-drug delivery systems and other clinical applications.

Keywords: Silver nanoparticles, Taverniera nummularia, Green synthesis, Antimicrobial activity, Antioxidant activity.

INTRODUCTION

In recent years, nanotechnology has become an important part of the scientific literature and is considered one of the most advanced technologies of today. It focuses on the production of nanoparticles (NPs) in various sizes and shapes within the nanometer range for the benefit of human health (1). In nanotechnology, the different properties, behaviors, and control of nanomaterials are examined in comparison with bulk materials (2). Due to their nanoscale size, NPs are used in many fields such as pharmaceuticals, the food packaging industry, open wound healing, and information technology (3), as well as in agriculture, food industries, chronic ulcer management, wound dressing, medicine, and cosmetics (4,5). Various types of nanoparticles have been developed, including copper (6), titanium–nickel (7), palladium (8), gold (9), and silver (10). Among these, silver nanoparticles (AgNPs) play an efficient role because of their strong antimicrobial effects against fungi (11), bacteria (12), and other eukaryotic microbes. They also function as theranostic agents (13) and possess antitumor properties (14). Colloidal silver particles possess desirable properties such as electrical conductivity, catalytic activity, chemical stability, and antibacterial effects (15). Silver ions exhibit a strong inhibitory effect against microbes and are considered permanent inhibitors (16). AgNPs are generally non-toxic to human cells when used in small amounts and may also be environmentally beneficial. Scanning electron microscopy (SEM) analysis has shown interactions between AgNPs and fungal cells, resulting in cell death due to membrane rupture (17).

Scientists show greater interest in AgNPs compared with other nanoparticles. These particles typically range from 1–100 nm in size, similar to the size of human body proteins. They play a significant role in surgical applications, wound care products, antioxidants, and antimicrobial agents (18). Through the reactivity of reactive oxygen species (O_2 species), AgNPs play an important role in cellular interactions and demonstrate inhibition comparable to the standard antioxidant drug ascorbic acid (19). Extracts of Myrtus communis have also been used to synthesize AgNPs that neutralize free radicals and enhance phenolic content (20).

However, conventional nanoparticle synthesis often involves toxic reducing agents and chemical solvents or surfactants, which may pose environmental and health risks (21). Large-scale synthesis of bulk materials can also generate harmful waste products during the nanoparticle production process (22). Therefore, biological and green synthesis methods are preferred for the biosynthesis of AgNPs, as plant extracts contain strong antioxidant phytochemicals that facilitate nanoparticle formation (23). In many cell types, AgNPs can induce necrosis or apoptosis (24). The genus Taverniera belongs to the family Fabaceae and is commonly found near small stream banks, particularly in saline soils (25). Taverniera nummularia leaves are used in poultices for sloughing wounds (26). Externally, the plant is used for treating swelling, ulcers, and abscesses (25). The roots are used orally for throat problems (27), and the seeds are used for the treatment of cough, while fried seeds are used to treat hoarseness of voice (28).

In this study, T. nummularia plant material was collected and processed to obtain an extract, which was subsequently used to synthesize silver nanoparticles (TN-AgNPs). The plant identity was confirmed, and a voucher specimen was deposited in the university herbarium. The extract was prepared by washing, drying, and grinding the plant material, followed by extraction with 80% methanol. The synthesized TN-AgNPs were characterized using various techniques, including UV–Vis spectrophotometry, X-ray diffraction (XRD), Fourier Transform Infrared Spectroscopy (FT-IR), and scanning electron microscopy (SEM). Factors affecting the synthesis process, such as pH and TN extract concentration, were also investigated. The results indicated successful synthesis and confirmed the crystalline nature and size of the TN-AgNPs. The antioxidant activities of TN-AgNPs were evaluated using DPPH, H_2O_2, and ABTS assays, demonstrating their potential as free radical scavengers. Furthermore, the antibacterial and antifungal activities of TN-AgNPs were assessed against various microbial strains, revealing significant inhibitory effects. Overall, this study highlights the green synthesis of TN-AgNPs and their potential applications in medicine and materials science.

METHODS

Plant Collection and preparation of extract

Taverniera nummularia, sourced from the township area of Bannu in KP, Pakistan, underwent botanical verification by Dr. Fizan Ullah Khan, Head of the Department of Botany at UST Bannu. A voucher specimen was duly archived in the university's herbarium. Upon identification, the entire plant was thoroughly washed with deionized water and left to air-dry in the shade for one month. Once fully dried, 1 kg of the plant material was finely ground into powder using a local grinder. Subsequently, 200 g of this powdered material was immersed in 80% methanol, subjected to agitation in a shaker for two days, and then filtered. The filtrate was brought to room temperature and concentrated using a Buchi Rota vapor R-200 evaporator. The resulting thick extract was measured and stored at 4°C for use in later experiments.

Synthesis of T. nummularia silver nanoparticles (TN-AgNPs)

With a minor modification, we employed established methods to synthesize silver nanoparticles (AgNPs) from plant materials (29). A 0.01 M silver nitrate solution was prepared by dissolving it in 50 mL of deionized water, which was then serially diluted tenfold by adding 1 mL of the solution to 9 mL of deionized water. Separately, 2 g of plant extract was dissolved in 100 mL of methanol, and the pH was adjusted using NaOH before the mixture was incubated overnight on a shaker. Another solution was prepared by mixing 1 mL of AgNO3 with 9 mL of deionized water, followed by pH adjustment with NaOH. Subsequently, 1 mL of the crude plant extract was added to the AgNO3 solution, and the mixture was allowed to react for 24 hours or until a brownish color appeared, indicating the formation of silver nanoparticles.

Factors affecting synthesis rate, size, and shape of AgNPs

We investigated several factors that could influence the formation of AgNPs, including pH, concentrations of silver nitrate and plant extract, temperature, and reaction time. The pH was adjusted from 8 to 12 using sodium hydroxide and hydrochloric acid, as it significantly affects nanoparticle size. By controlling the pH, we were able to modulate the size of the nanoparticles (30). Different volumes of plant extract, ranging from 100 to 1000 μL, were also tested to evaluate their effect on nanoparticle formation. Variations in silver nitrate concentration similarly influenced the size and morphology of the nanoparticles, with higher concentrations yielding smaller nanoparticles and lower concentrations producing larger ones. Our primary objective was the eco-friendly synthesis of silver nanoparticles using the plant extract (31).

Characterization of Silver AgNPs

The concentration of TN-AgNPs synthesized via green methods was measured using a SHIMADZU UV SPECTROPHOTOMETER (UV-1800). The presence of various phytochemicals in the purified TN-AgNPs and TN-extract was analyzed using a Fourier Transform-Infrared (FT-IR) spectrometer (Shimadzu, IR Prestige-21, Japan). The crystalline nature of TN-AgNPs and TN-extract was examined using an X-ray diffractometer (XRD) (Model D-8 Advance, Germany) with a wavelength of 1.54 Å. The size and morphology of TN-AgNPs were determined using a JEOL Scanning Electron Microscope (SEM) (MIRA3 TESCAN model). Additionally, Energy-Dispersive X-ray spectroscopy (EDX) was employed to confirm the presence of elemental silver in the TN-AgNPs.

Activities of in vitro antioxidants:

1,1-diphenyl-2-picrylhydrazyl Activity

A 3 mg amount of 1,1-diphenyl-2-picrylhydrazyl (DPPH) was accurately weighed and dissolved in 50 mL of methanol. The initial absorbance of the DPPH solution at 0.765 nm was determined using Formula 1. The free radical scavenging activity of the plant extract, AgNPs, and ascorbic acid was evaluated using a modified method adapted from Brand-Williams, Cuvelier, & Berset, 1995 (32). A stock solution of the plant extract (1 mg/mL in water) was prepared, which also included the silver nanoparticles and ascorbic acid. Serial dilutions were then made to obtain concentrations of 20, 40, 80, and 100 μg/mL. For each concentration, 100 μL was mixed with 900 μL of DPPH solution in separate test tubes, thoroughly shaken, and incubated in low light for 30 minutes. The absorbance was measured at 517 nm using water as a blank. The percentage of DPPH inhibition was calculated by comparing the absorbance after reaction with the original DPPH absorbance.

% Scavenging=Ac-As/Acx 100 1

Ac = Controlled absorbance

As = Sample absorbance

H_2O_2 Scavenging Activity

The method described by Pick & Mizel, 1981 (33) was slightly modified. A 50 mM phosphate buffer (pH 7.4) containing 2 mM hydrogen peroxide was prepared. Various concentrations (20, 40, 80, and 100 μg/mL) of ascorbic acid, silver nanoparticles, and plant extract were tested. For each sample, 0.2 mL was mixed with 0.6 mL of hydrogen peroxide and 0.4 mL of phosphate buffer. The mixtures were shaken, and absorbance was measured at 230 nm after 15 minutes. For samples with an initial absorbance of 0.81, the hydrogen peroxide scavenging activity of silver nanoparticles and plant extract was calculated.

ABTS Radical Scavenging Activity

The ABTS assay was performed based on Mathew & Abraham, 2006 (34) with minor modifications. A stock solution was prepared by mixing equal volumes of 7 mM ABTS and 2.45 mM potassium persulfate and incubated in darkness at 37°C for 24 hours to generate ABTS radicals. The stock solution was then diluted with 50% methanol to prepare the working solution. At 30°C, the initial absorbance was approximately 0.936. Different concentrations (25, 50, 75, and 100 μg/mL) of the plant extract were tested by adding 0.2 mL of each concentration to 0.8 mL of ABTS solution (initial absorbance 0.836). After 6 minutes of mixing, the decrease in absorbance was recorded. The experiment was performed in duplicate, with ascorbic acid as a positive control.

Antimicrobial Screening of AgNPs

The antibacterial activity of silver nanoparticles was evaluated against Staphylococcus aureus, Escherichia coli, and Klebsiella pneumoniae. S. aureus showed no inhibition, whereas E. coli and K. pneumoniae (Gram-negative) were affected. Nutrient agar was prepared by dissolving 7 g of nutrient agar powder in 250 mL distilled water (pH 7), autoclaved, and cooled to 45°C. Plates were poured with 40 mL of agar under sterile conditions. Fresh bacterial cultures were spread using sterile cotton swabs, and four wells were made in each plate using a cork borer. A 1 mg/mL stock solution of AgNPs was prepared and further diluted to 150 and 300 μg/mL for testing. Erythromycin served as a positive control and DMSO as a negative control. Plates were incubated at 37°C for 24 hours, and inhibition zones around the wells were measured to assess antibacterial activity at different concentrations.

RESULTS

Concentration Study

AgNPs were synthesized by utilizing a plant extract. Ten solutions were prepared by combining a pH 11 $1x10^{-3}$ M AgNO3 solution. Subsequently, varying volumes of methanolic plant extract solution ranging from 100 µL to 1 ml were added to these solutions. After a 24-hour incubation period, the color of these solutions transformed to a yellowish-brown, indicative of the successful synthesis of AgNPs.

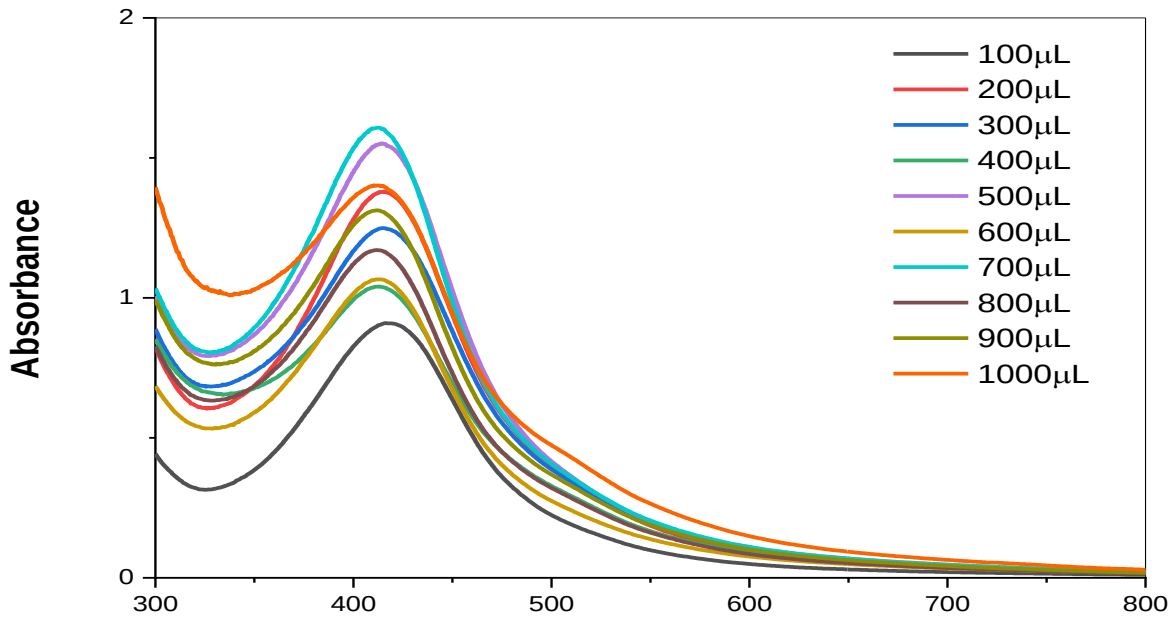

Figure 1. Impact of Taverniera nummularia plant extract concentration on the synthesis of AgNPs.

UV-visible spectrophotometric analysis of TN-AgNPs

The TN-AgNPs aqueous solution show yellowish brown colour due to surface plasmon resonance (SPR). The mixing of TN- extract and $AgNO_3$ solution the appearance of light brown colour indicate the Ag^+ bio reduction by the TN active molecules. At the range of 200 – 800 nm at a temperature of 40C, after 24 hr. incubation, pH 11, 1mM salt concentration and 1mL TN- extract concentration spectrophotometer indicate a peak of 2.0 At absorbance of 407 nm for the TN- AgNPs.

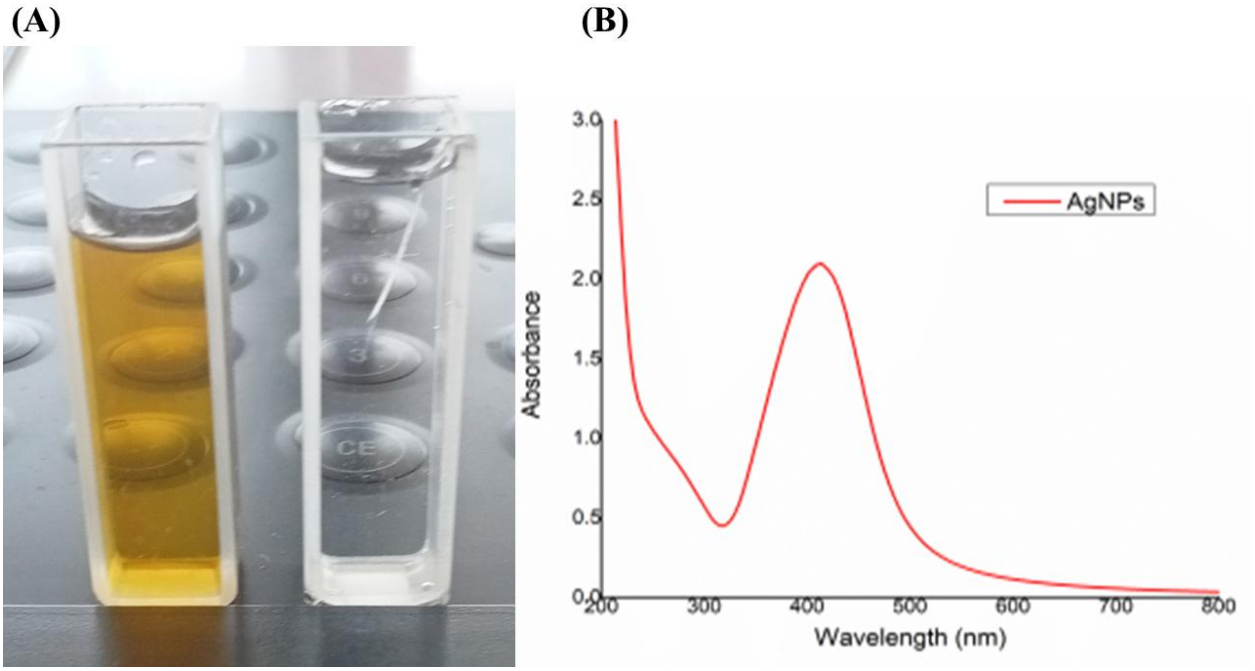

Figure 2. (A) Yellowish brown colour of AgNps. (B) The UV-vis absorption spectrum of TN-AgNPs

FT-IR analysis of TN-extract and TN-AgNPs

Fourier Transform Infrared(FTIR) spectrum analysis of TN-extracts and AgNPs (Silver Nanoparticles) prepared in water. The analysis involves identifying peak values and probable functional groups present in the TN-extracts and AgNPs. The characteristic absorption band were demonstrated in the range exist in FTIR chart. The observed FTIR peaks of TN-extracts and AgNPs values were compared to standard values in the FTIR chart to identify the exact functional groups responsible for the bio reduction process. Figure 4 showed peaks at 3772, 3415, 2957, 2568, 2262, 2147, 1638, 861, and 644 cm^{-1} by TN-extracts. 3766, 3510, 3167, 2606, 2153, 1714, 1440, 1045, and 765 cm^{-1} by AgNPs. Different functional groups correspond to these peaks. The peak at 3772 and 3766 in FT-IR indicates that there must O-H group of alcohol compounds; peak at 3415, 3510 and 3167 cm^{-1} corresponded to N-H stretching functional group of primary amine, aliphatic primary amine, and secondary amine; 1714, 1638, and 1440 cm^{-1} band corresponds to C=O stretching correspond to carboxylic acid, C=C stretching correspond to alkene and O-H bending correspond to carboxylic acid respectively. Different vibrating stretching of functional groups correspond to all other peaks.

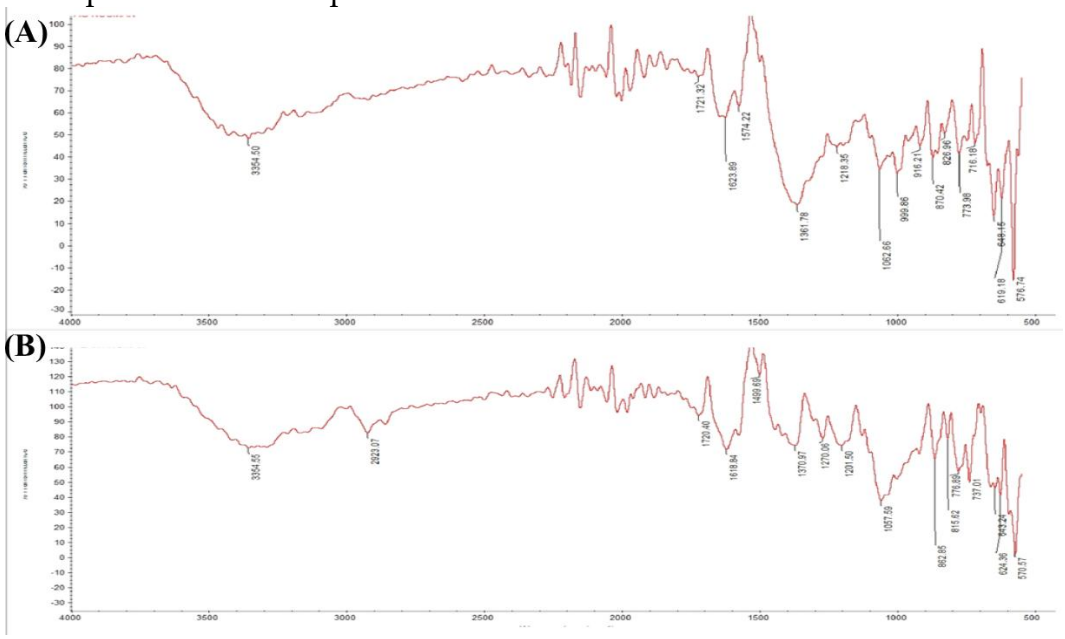

Figure 3. FTIR analysis of (A) TN-extract (B) AgNPs

XRD analysis of TN-AgNPs

The sample of TN-AgNPs were analyzed by XRD. Figure 3. show Bragg reflections at angles of 38.21(111), 46.29(200), 64.64(220), and 77.55(311) showed the varius diffrection peaks respectively (Sathiyaraj et al., 2021). The face-centered cubic crystal structure of the silver ions in these reflections can be confirmed by indexing the faces. Interplanar spacing (d) and Miller constants (a) values are then calculated using Debye-Sherrer's equations 3 and 4 respectively:

$$Dhkl = \frac{\pi}{2\mathrm{Sin}\theta\mathrm{hkl}} \quad (3)$$

$$å = dhkl\ (h2 + k2 + l2)1/2 \quad (4)$$

By using Debye-Sherrer's formula 5, the average crystalline size of TN-induced AgNPs is calculated

$$D = \frac{K\lambda}{\beta\cos\theta} \quad (5)$$

D = the average crystalline size,

k = geometric factor (0.9),

λ = wavelength of the X-ray radiation source, and

β = angular FWHM (full-width at half maximum) Here is a more casual summary:

To calculate the average crystal size of the silver nanoparticles, we measured the full-width at half maximum (FWHM) of some of the major peaks in the XRD pattern. Specifically, we looked at the peaks around 38.21°, 46.29°, 64.64°, and 77.55°. The FWHM is related to the crystalline size by a formula that

includes the Bragg diffraction angle (θ). By plugging in the FWHM and θ values for each of those 4 peaks, we were able to calculate the crystalline size. The average size we calculated from those peaks was around 110 nanometers. So based on the XRD analysis, the silver nanoparticles produced had an average crystalline domain size of 110 nm.

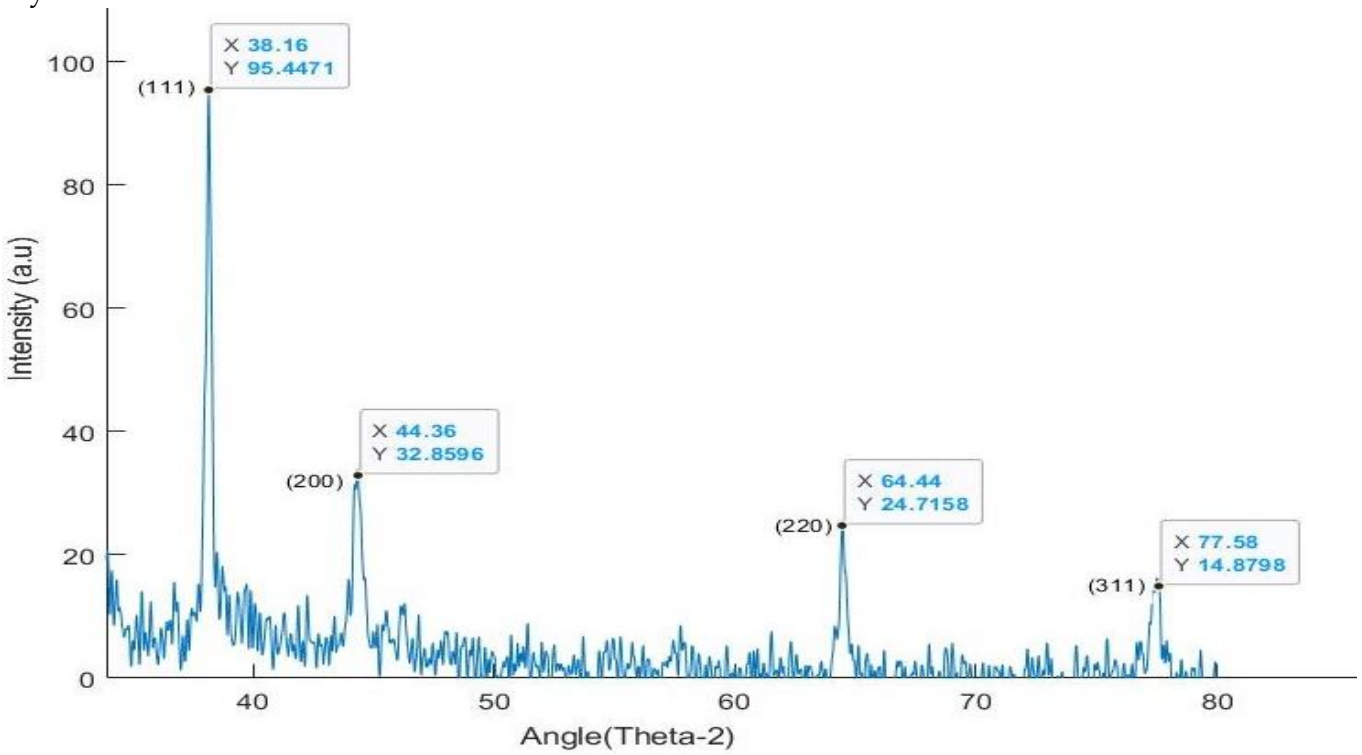

Figure 4. XRD analysis for Taverniera nummularia-derived AgNPs.

SEM analysis of TN-AgNPs

SEM was used to examine the surface morphology of TN-AgNPs. The SEM findings reveal that TN-AgNPs exhibit a monodispersed and spherical-shaped structure, reaching maximum density (Figure 5). The average particle size was determined using Nano Measurer software by analyzing 100,000 particles and was found to be 0.1 nm.

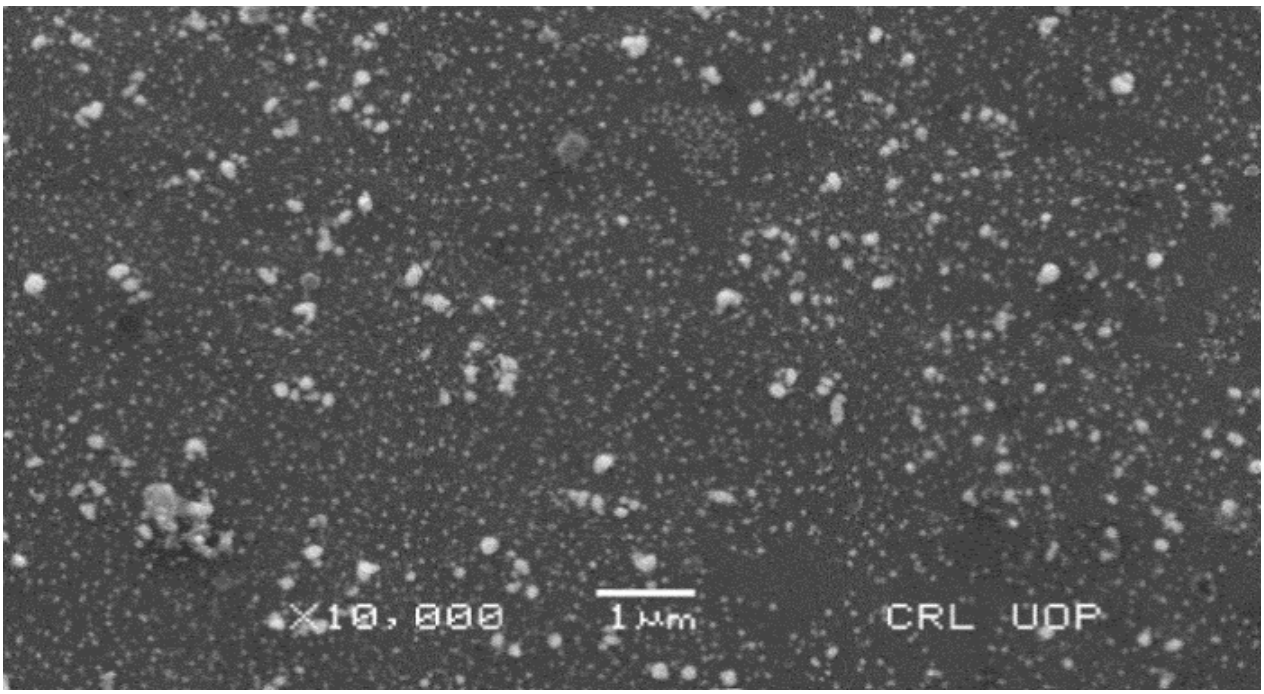

Figure 5. SEM examination of AgNPs made from plant extract of *Taverniera nummularia*.

Antioxidant assays

DDPH scavenging assay

The antioxidant capability of the produced AgNPs was assessed through the DPPH activity method as outlined by Brand-Williams et al. (35). As a reference, ascorbic acid, a well-known free radical scavenger, demonstrated the highest inhibition in Figure 6 (blue bars). Notably, the synthesized AgNPs exhibited superior antioxidant properties compared to the plant extract alone, with the gray bar indicating plant extract inhibition and the yellow bar representing nanoparticles. The figure illustrates the DPPH activity using AgNPs synthesized from the plant extract of TM.

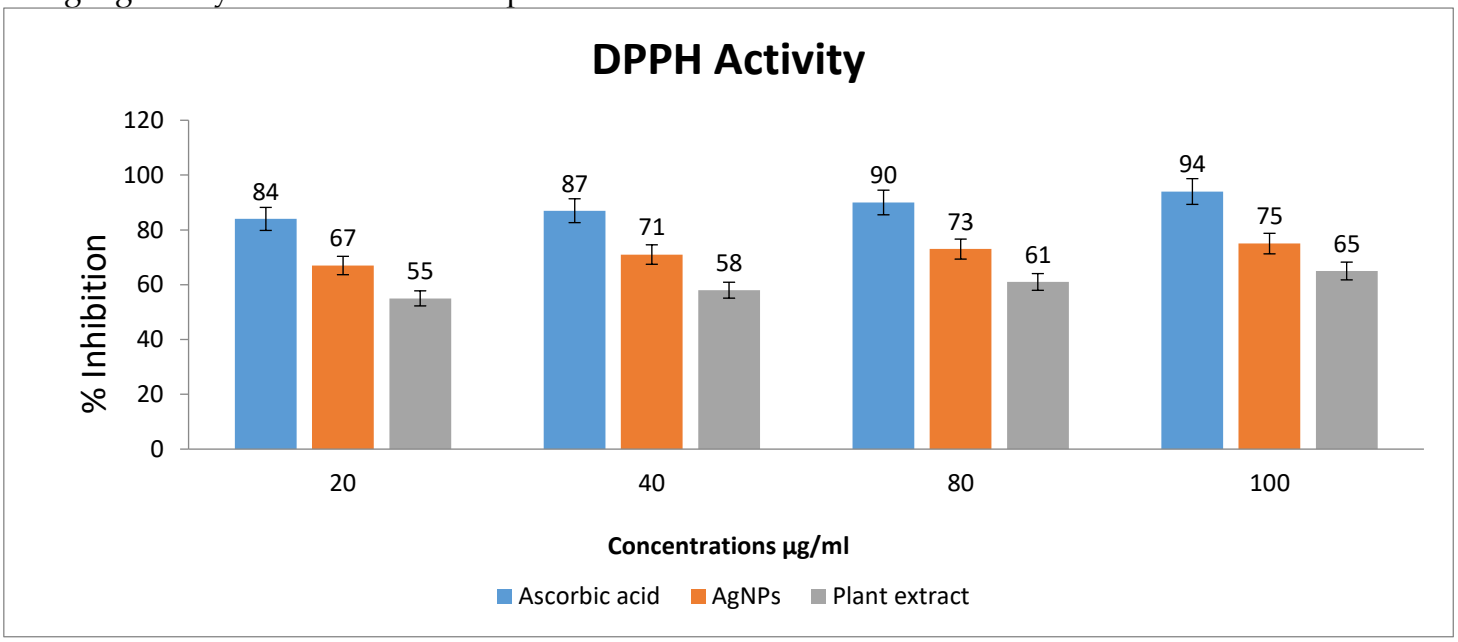

Figure 6. Evaluating the effectiveness of ascorbic acid, synthetic AgNPs, and *Taverniera nummularia* plant extract in scavenging DPPH free radicals.

Hydrogen peroxide scavenging (H_2O_2)

For the evaluation of hydrogen peroxide scavenging activity, we utilized a modified version of Pick & Mizel (36). AgNPs and plant extracts both demonstrated free radical scavenging abilities, with ascorbic acid exhibiting the highest capacity for scavenging free radicals.

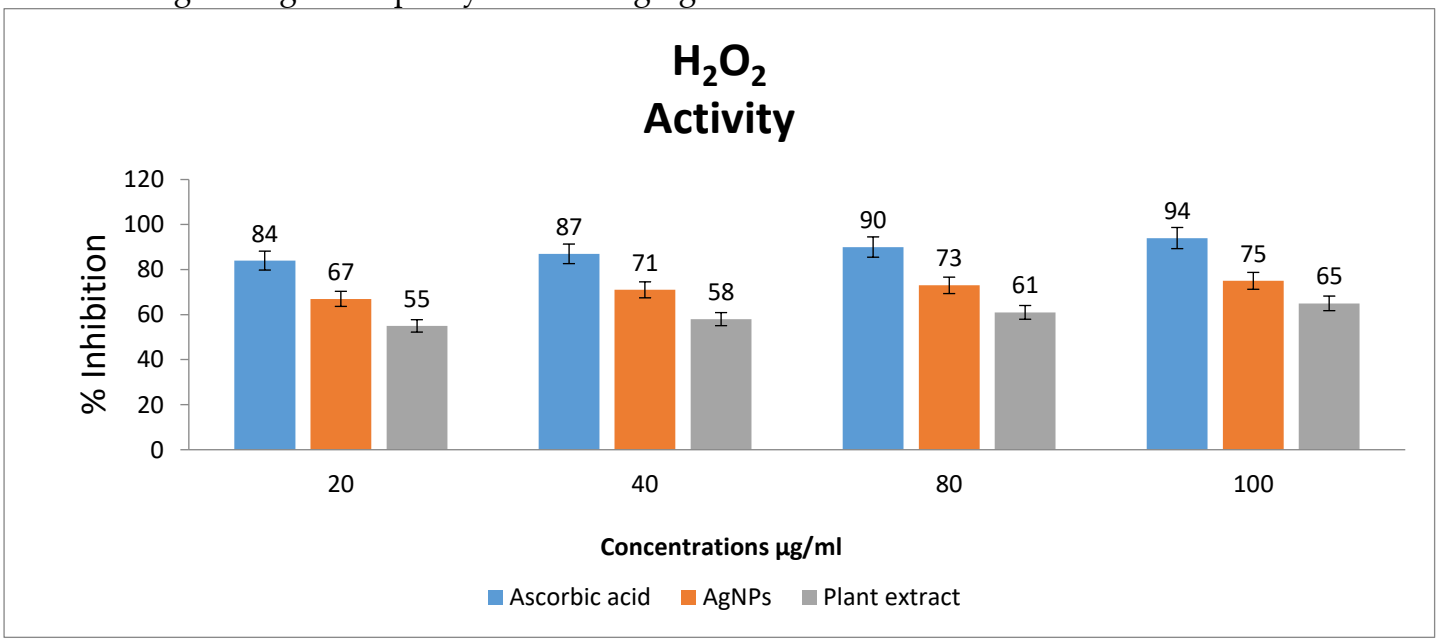

Figure 7. Evaluating the scavenging activity of hydrogen peroxide free radicals.

ABTS screening assay

ABTS is used similarly to DPPH to measure antioxidant effects. We made an ABTS stock solution and diluted it. Then mixed different amounts of the test samples with the ABTS and measured any decrease in absorbance over time. A lower final absorbance means more ABTS radicals were scavenged, indicating better antioxidant effects. We did this with some modifications to the typical ABTS method given by Mathew & Abraham, 2006).

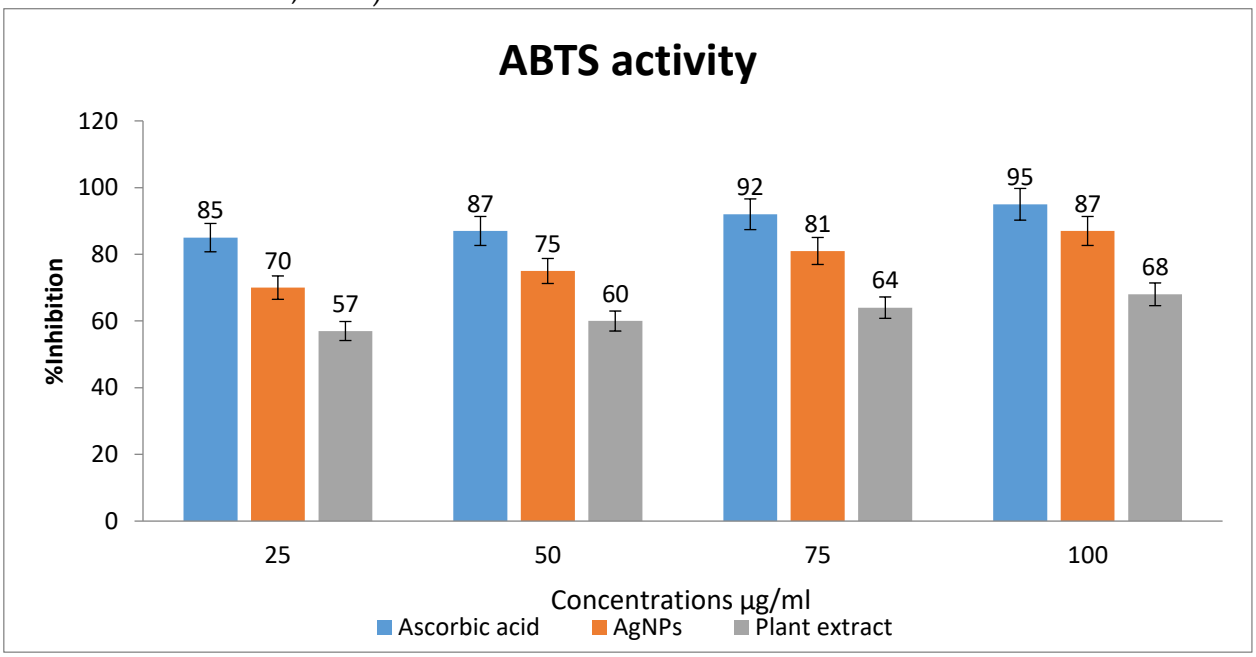

Figure 8. Ascorbic acid, AgNPs, and a *Taverniera nummularia* plant extract demonstrate ABTS free radical scavenging capabilities.

In-vitro antifungal and antimicrobial activities

We tested different concentrations of AgNPs and the TN plant extract against fungal and bacterial strains. For fungi, both 150 and 300 µg/mL of AgNPs and TN showed significant inhibition compared to the control, with AgNPs inhibiting more (zones 30-41 mm vs 39-57 mm for TN). For bacteria, AgNPs also exhibited stronger antimicrobial activity than TN based on larger inhibition zones (12-20 mm vs 3.4-9.1 mm). Both AgNPs and TN were effective against all strains tested. DMSO was negative and levofloxacin/terbinafine positive controls confirmed the results. So in summary, AgNPs and TN demonstrated notable antifungal and antibacterial properties in this study.

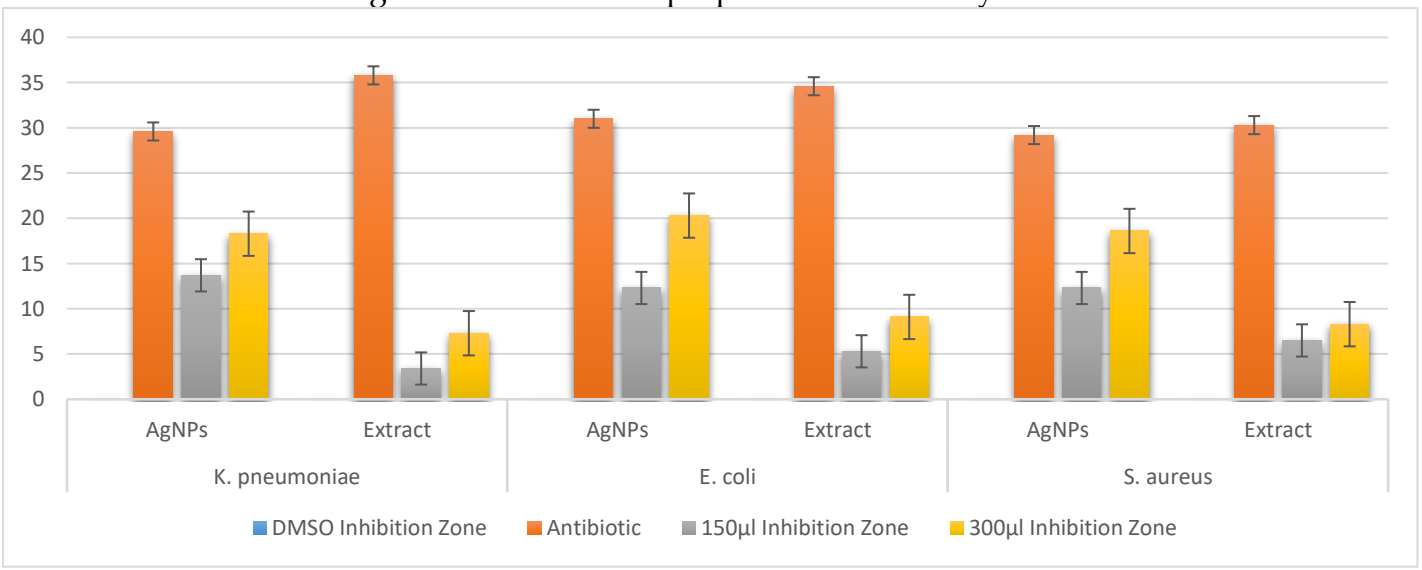

Figure 9. The antibacterial properties of *T. nummularia* plant extract and synthesized AgNPs were observed against the three bacterial strains.

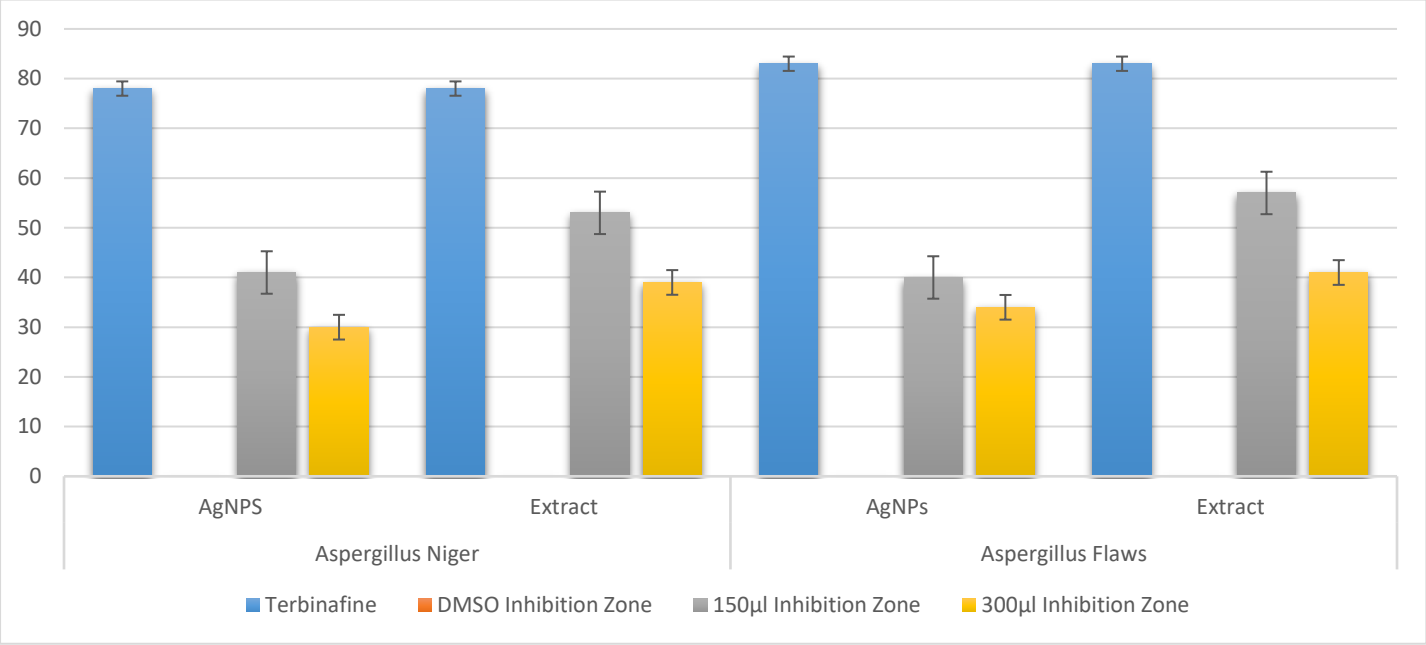

Figure 10. The antifungal activity of the plant extract and the synthesized silver nanoparticles from *T. nummularia* was assessed against the aforementioned fungal strains.

DISCUSSION

This study looked at synthesizing AgNPs using T. nummularia leaf extract, which has potential benefits in pharmaceuticals. The synthesis of AgNPs involved the use of silver nitrate as the reducing agent and leaf extract as the starting material. We investigated various factors that influence AgNP formation. Factors like temperature, silver nitrate concentration, the ratio of leaf extract to silver nitrate solution, pH, and reaction time were considered. The confirmation of AgNP formation involved identifying the functional groups responsible for reducing silver nitrate and the capping agents present in the leaf extract. The leaf extract used in AgNP synthesis was then characterized using UV-Vis spectroscopy, FTIR, EDS, and TEM to analyze its properties and composition. The goal was to optimize the AgNP synthesis process using this leaf extract as a natural, eco-friendly method.

The antibacterial activity of the produced AgNPs against Escherichia coli (E. coli) was also investigated. The research demonstrated that the synthesized AgNPs from T. nummularia exhibit a spherical shape, as confirmed by SEM analysis. FTIR analysis revealed the presence of various phytochemical components in the plant extract, contributing to the stability and mediation of nanoparticles. It was found that FTIR analysis is a valuable tool for identifying functional groups, and the results indicated the existence of hydroxyl, carboxyl, and amide groups, which play a crucial role in reducing metal ions to produce nanoparticles, as supported by previous scientific studies (37,38). Green-synthesized nanoparticles and phyto-components play a significant role in nanoparticle stabilization and exhibit applicative properties (39).

The crystalline structure and size of AgNPs were analyzed using X-ray diffraction (XRD), revealing distinct diffraction peaks at 2Θ values of 38.16° (111), 44.36° (200), 64.48° (220), and 77.56° (311). These peaks confirmed the crystalline nature of the produced particles and indicated an average size of approximately 110 nm. XRD analysis of TN-AgNPs unveiled four distinct peaks, providing additional confirmation of the crystalline nature of the AgNPs. Consistent findings were reported in previous studies (40).

The antioxidant properties of AgNPs synthesized from T. nummularia plant extract were assessed using the DPPH assay and ROS determination techniques. No unfavorable inflammatory responses were observed. Chitosan, chosen for its beneficial biological characteristics such as non-toxicity, biocompatibility, biodegradability, and antibacterial capacity, also serves as a cell proliferation booster and drug delivery carrier.

The DPPH activity test utilized AgNPs derived from the T. nummularia plant extract as a baseline to assess the antioxidant capability of the synthesized AgNPs. Ascorbic acid served as a standard reference because of its outstanding free radical scavenging properties. Increasing concentrations of AgNPs, plant extract, and ascorbic acid enhanced their efficiency in scavenging free radicals. At a concentration of 100 µg/mL, ascorbic acid demonstrated 98% activity, outperforming both plant extract (67%) and AgNPs (79%). Both AgNPs and plant extract exhibited the ability to scavenge free radicals, with AgNPs showing superior scavenging activity compared to the plant extract (41). The addition of AgNPs to the solution caused a color change, representing the donation of

electrons to DPPH, which stabilizes the radical (Molyneux, 2004). The efficiency of the green-synthesized AgNPs was attributed to the presence of various phytochemicals in the extract (42).

Hydrogen peroxide, an inorganic and highly reactive oxidant, is known to cause severe damage to the cell membrane of living systems. In the current study, the hydrogen peroxide assay was conducted using different concentrations of AgNPs and TN-extract ranging from 20 to 100 µg/mL. The results revealed 94%, 75%, and 64% inhibition by ascorbic acid, AgNPs, and TN-extract, respectively, at the highest concentration of 100 µg/mL. This study aligns with previous research on AgNPs derived from Iresine herbstii, indicating enhanced antioxidant and biological activities (43). Relative to previous results (44), ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)) exhibits significant potential in scavenging free radicals, with maximum absorbance typically observed at 734 nm. In the current study, a decrease in absorbance was noted with increasing concentrations of AgNPs (45). The scavenging ability of bio-synthesized AgNPs and TN-extract against the ABTS free radical was evaluated. The results demonstrated an effective free radical % scavenging potential of 86% for AgNPs and 69% for TN-extract (46). Numerous studies have focused on silver nanoparticles (AgNPs) to augment the antibacterial features of medical items, particularly wound dressings. Research has explored integrating AgNPs into chitosan-based membranes to assess their impact on wound healing efficacy. Notably, AgNPs demonstrated substantial antimicrobial activity against both Gram-positive and Gram-negative bacteria, with the most significant zone of inhibition observed against Gram-negative bacteria (47). The synthesized TN-AgNPs extract was assessed for its antibacterial properties using three bacterial strains—Klebsiella pneumoniae, Escherichia coli, and Staphylococcus aureus. The zones of inhibition (mm) exhibited by AgNPs were measured, with the most effective performance observed at a concentration of 300 µg/mL AgNPs. Klebsiella pneumoniae demonstrated the greatest zone of inhibition, specifically 18.3 ± 0.78 mm. The study also suggests the potential use of AgNPs as an antifungal agent in drug therapy for human infections (Panácek et al., 2009). Different concentrations of AgNPs on various fungal strains showed significant growth inhibition, as reported previously (48).

CONCLUSION

The recent experimental findings highlight the promising potential of *Taverniera nummularia* (*T. nummularia*) as an efficient and environmentally friendly method for the rapid synthesis of silver nanoparticles, offering versatility for various clinical applications. In-depth analysis via Fourier Transform-Infrared (FT-IR) spectroscopy indicates that the crude methanolic extract from *T. nummularia* exhibits key functional groups essential for nanoparticle synthesis. The resulting silver nanoparticles, as evidenced by X-ray diffraction (XRD) and scanning electron microscopy (SEM), display crystalline properties and distinctive aggregate characteristics. Moreover, the synthesized silver nanoparticles demonstrate noteworthy antimicrobial activity, showing significant efficacy against both bacterial and fungal strains. Additionally, they exhibit substantial antioxidant properties, with strong free radical scavenging capabilities. These findings underscore the multifaceted applications and promising attributes of *T. nummularia* in silver nanoparticle synthesis, contributing to advancements in both medical and environmental domains.

Conflict of Interest

Authors declare no conflict of interest.

Ethical consideration

The study was approved by local research ethics committee.

Author contributions

SNS conceptualization and experiments, YMH supervise and review it. OA review and manage the writing scientifically.

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Original Article

Impact of Yogic Ocular Exercises on Near Point of Convergence in Young Adults with Convergence Insufficiency: A Quasi-Experimental Study

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ABSTRACT:
This study was conducted to determine the effect of yogic ocular exercises on convergence insufficiency by measuring changes in near point of convergence (NPC) over six weeks. This quasi-experimental study was carried out at the University of Lahore Teaching Hospital from July to August 2025 after ethical approval (IRB UOL/IREB/25/0009). Forty-seven participants (31 females, 16 males) aged 18–26 years with clinically diagnosed convergence insufficiency were enrolled. NPC was assessed using a RAF ruler at baseline, three weeks, and six weeks. Participants performed daily yogic ocular exercises—including palming, blinking, sideways, rotational and diagonal viewing, nose-tip gazing, near–distant viewing, concentrated gazing, candle flame gazing, and acupressure stimulation—for 30 minutes over six weeks. Friedman and Wilcoxon signed-rank tests were used for statistical analysis. The mean age of participants was 22.55 years. Baseline NPC ranged from 11.0 to 15.5 cm with a mean of 11.55 cm. After three weeks of exercises, the NPC improved with a mean of 10.78 cm (range 7.5–15.0 cm), and after six weeks, the NPC further improved to a mean of 9.81 cm (range 7.5–13.5 cm). The reduction in NPC over time was statistically significant ($p < 0.001$). Regular practice of yogic ocular exercises significantly improved NPC and may help reduce visual discomfort associated with convergence insufficiency. These exercises could be considered an effective, low-cost, non-invasive adjunct to conventional management in young adults.

Keywords: Convergence insufficiency, near point of convergence, yogic ocular exercises, binocular vision, non-invasive therapy

INTRODUCTION

The eyes are specialized sensory organs that can be considered as living optical devices. They have complex functions and anatomy that enable them to receive visual images by constantly adjusting the amount of light entering the eye and adjusting the focus of the eye at near and far distances. These visual images are then instantly transmitted to the brain. For the visualization of these images, eyes collect light from the surrounding environment by moving in different directions and planes. These movements are carried out by the six extraocular muscles that control the movements of the eye in different directions. An abnormality in the medial rectus and lateral rectus muscles can cause convergence insufficiency (1). It is an important mechanism to achieve binocular single vision (2). Convergence can be affected by different factors such as reading and other near activities. It can also occur due to unstable conditions like bright light, constant working time, short working distance, excessive use of electronics, uncorrected refractive errors, accommodative and binocular anomalies, and mental status (3). The anomalies of convergence are convergence insufficiency, convergence paralysis, and convergence spasm. CI is a well-defined binocular vision disorder with a reported prevalence among all age groups in the United States of 2.25% to 8.30%. Convergence insufficiency can be idiopathic or can be the result of refractive errors, presbyopia, muscular imbalance, and consecutive convergence insufficiency (4).

Its symptoms include asthenopia, diplopia, nausea, headache, and blurry vision, generally associated with activities that require near vision. The normal value of near point of convergence is 7–10 cm. More than 10 cm is considered as convergence insufficiency (5). With the help of different treatments, we can relieve convergence insufficiency and its complications (6). There are multiple treatment options to treat convergence insufficiency such as optical treatment, orthoptic treatment, prismotherapy, and surgery (7).nOrthoptic treatments include many therapies such as pencil push-up exercises, which are used to improve convergence insufficiency (CI). They are also used to correct binocular visual disorders (strabismus). Other than the orthoptic exercises, another set of exercises called yogic ocular exercises are also expected to be a treatment option for the improvement of convergence insufficiency. The practice of yoga is also becoming popular in Western societies (8). Various online videos, yoga practitioners, and

online websites recommend yogic ocular exercises and their multiple effects on eyes, such as reduction in ocular fatigue and improvement in the movement of eyes. These exercises are not only beneficial for the reduction of ocular fatigue and intraocular pressure (9) but also improve vergence facility, binocular accommodative facility, and fusional vergences (10). Despite the growing popularity of yogic ocular exercises, most available studies focus on general eye fatigue or intraocular pressure rather than convergence-specific outcomes. Furthermore, existing evidence is largely descriptive, with few controlled or quasi-experimental investigations evaluating their direct impact on near point of convergence. Consequently, the therapeutic potential of these exercises for patients with convergence insufficiency remains unclear

In yogic ocular exercises, extraocular muscles continuously contract and relax in different directions. This increases oxygen consumption of ocular muscles, which leads to increased intraorbital blood flow. Thus, it improves the muscular tone of extraocular muscles, resulting in improvement of convergence insufficiency. It commonly consists of a set of 10 exercises, which are front sideways viewing, sideways viewing, rotational viewing, diagonal viewing, preliminary nose-tip gazing, near and distant viewing, concentrated gazing, acupressure points on the palm, blinking, and palming (11).

A review-based study was carried out in 2021 by *Ayunda Puteri Rizanti* to ascertain the effects of yogic ocular exercises on reducing eye fatigue and boosting ocular health. Through a review of eight articles that were selected, they discovered that yogic ocular exercises can help glaucoma patients by lowering their intraocular pressure, reducing eye strain, calming the mind, preventing asthenopic symptoms, and improving binocular vision. The author concluded that yoga and trataka exercises have no negative side effects and can be utilized as an intervention to preserve eye health in the modern age (12).

Senthil Kumar carried out another scriptural and academic evaluation study in 2022. The study showed a beneficial effect on the regulation of autonomic functions, improvement of cognitive functions, reduction of eye-related discomfort, and enhancement of joy and mental peace (13). In 2022, another study was conducted by Tommaso Bianchi and Raffaella Bellen to find out whether eye yoga activities have immediate effects on morphoscopic visual acuity. The average improvement in visual acuity was 2.28%, indicating that yogic exercises were effective in improving vision (14). This study will aid eye care practitioners in exploring a novel technique in the treatment of convergence insufficiency. It will help eye care practitioners to discover non-pharmacological and therapeutic treatments to relieve convergence-insufficiency-related anomalies of binocular vision function.

METHODS

A quasi-experimental study was carried out at the University of Lahore Teaching Hospital, Lahore, Pakistan, from July to August 2025. Forty-seven participants aged 18–26 years diagnosed with convergence insufficiency (NPC > 10 cm and symptomatic exophoria at near) were enrolled. Exclusion criteria included hyperopia > +1.00 D, astigmatism, strabismic anomalies, systemic medications affecting vision, or prior orthoptic therapy. Ethical approval was obtained from the University of Lahore Ethics Committee (UOL/IREB/25/0009). Informed consent was secured from all participants.

Participants performed 10 yogic ocular exercises daily for 30 minutes over six weeks, including palming, blinking, sideways viewing, rotational viewing, diagonal viewing, front and sideways viewing, preliminary nose-tip gazing, near-distant viewing, concentrated gazing, and acupressure stimulation. Exercises were supervised weekly. NPC was measured using the RAF ruler at baseline, after three weeks, and after six weeks. Symptom frequency (headache, eye strain, diplopia, blurred vision) was recorded via a structured questionnaire.

Statistical analysis was conducted using SPSS v25. The Friedman test was used to assess within-group changes, and the Wilcoxon signed-rank test compared pre- and post-intervention outcomes. A p-value < 0.05 was considered statistically significant.

RESULTS

Forty-seven participants completed the study evaluating near point of convergence (NPC) improvements using the RAF ruler over 6 weeks. No participants were lost to follow-up, ensuring complete data for primary (NPC measurements) and secondary (symptom frequency) outcomes. The study population was predominantly female (31/47, 66.0%), with 16 males (34.0%). The mean age was 22.0 ± 2.5 years (range not specified in data), reflecting a young adult cohort suitable for convergence insufficiency assessment.

Primary Outcome: NPC Measurements

At baseline, mean NPC was 11.5 ± 1.5 cm, with a range of 8.0–15.5 cm, indicating initial convergence deficits consistent with study inclusion criteria. Following 3 weeks of intervention, mean NPC decreased to 10.8 ± 1.6 cm (range: 7.5–15.0 cm), representing an absolute reduction of 0.7 cm. By 6 weeks, further improvement occurred, with mean NPC at 9.8 ± 1.5 cm (range: 7.5–13.5 cm), a total reduction of 1.7 cm from baseline. These temporal changes are summarized in Table 1, and baseline normality is depicted in the Q-Q plot (Figure 1).

Statistical Significance of NPC Changes

Non-parametric analysis was applied due to data distribution. The Friedman test across all time points yielded a p-value of <0.001, indicating significant overall change. Pairwise Wilcoxon signed-rank tests revealed highly significant improvements: baseline versus 3 weeks (Z = -5.311, p = 0.001), baseline versus 6 weeks (Z = -5.877, p = 0.001), and 3 weeks versus 6 weeks (Z = -5.786, p = 0.001). Effect sizes were large (Z > 5 in absolute value), supporting robust intervention effects, as shown in Table 2 and Figure 2-3.

Secondary Outcome: Convergence Insufficiency Symptoms

Pre-intervention symptom frequencies were assessed across eight domains using a 5-point scale (none of the time to all of the time). Baseline means ranged from 0.94 ± 1.187 (redness) to 2.02 ± 1.132 (blurry vision or headache), with most participants reporting symptoms "some" to "most" of the time. Post-intervention (6 weeks), all domains showed reduced frequencies and means; for instance, headache improved from 2.02 ± 1.032 to 1.09 ± 0.905, with "none of the time" increasing from 2 to 14 participants. Eyestrain and redness exhibited the largest proportional shifts, with "none" rising to 25/47 and 33/47, respectively. Tired eyes, irritation, burning, and double vision also trended toward less frequent reporting, though blurry vision showed milder change (mean 2.02 to 1.28). Comprehensive frequencies and means are presented in Table 3.

Table 1. Near Point of Convergence (NPC) Measurements (n = 47)

Measurement	Mean ± SD (cm)	Range (cm)
Baseline	11.5 ± 1.5	8.0 – 15.5
3 weeks	10.8 ± 1.6	7.5 – 15.0
6 weeks	9.8 ± 1.5	7.5 – 13.5

Table 2. Pairwise Comparisons of NPC Measurements (Wilcoxon Signed-Rank Test)

Comparison	Test Statistic	*p*-value
Baseline vs. 3 weeks	Wilcoxon Z = -5.311	<0.001
Baseline vs. 6 weeks	Wilcoxon Z = -5.877	<0.001
3 weeks vs. 6 weeks	Wilcoxon Z = -5.786	<0.001

Table 3. Symptom Frequencies and Means Pre- and Post-Intervention (n=47)

Pre- Intervention							Post Intervention					
	None of time	Some of time	Half of time	Most of time	All of time	Mean	None of time	Some of time	Half of time	Most of time	All of time	Mean
Headache	2	16	10	17	2	2.02 ± 1.032	14	18	12	3	0	1.09± 0.905
Tired eyes	1	20	8	15	3	1.98±0.153	14	17	12	4	0	1.13± 0.947
Eyestrain	19	15	6	6	1	1.04±1.122	25	15	4	2	1	0.70±0.954
Irritation	5	21	9	12	0	1.60±0.993	15	20	11	1	0	0.96±0.806
Blurry	3	16	9	15	4	2.02±1.132	11	18	13	4	1	1.28±0.994
Burning	16	17	8	5	1	1.11±1.068	25	18	3	1	0	0.57±0.715
Redness	25	8	7	6	1	0.94±1.187	33	9	4	1	0	0.43±0.744
Double	9	13	10	12	3	1.72±1.228	15	16	12	3	1	1.13±1.013

DISCUSSION

The present study evaluated the effect of yogic ocular exercises on convergence insufficiency among young adults attending the University of Lahore Teaching Hospital. A total of 47 participants, including both male and female emmetropes aged 18–26 years with asthenopic symptoms and convergence insufficiency primarily due to muscular imbalance, were included. Participants with systemic disease, prior ocular treatment, or strabismus were excluded to minimize confounding factors. Near point of convergence (NPC) was assessed using a RAF ruler at baseline, three weeks, and six weeks following a structured yogic ocular exercise regimen.

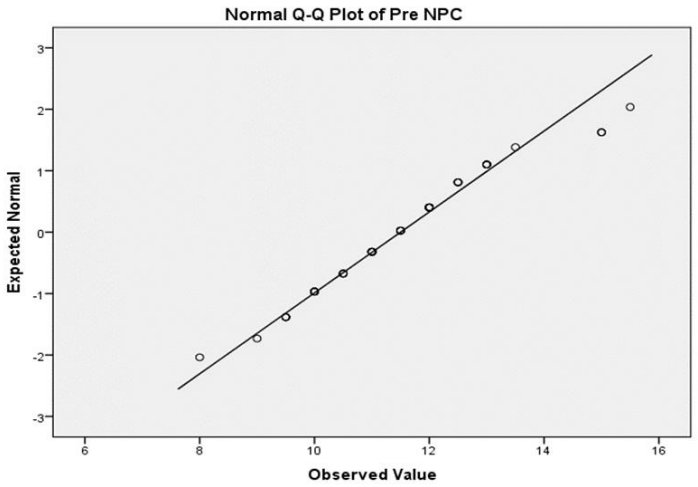

Figure 1: Q-Q Plot of Pre near point of convergence (NPC)

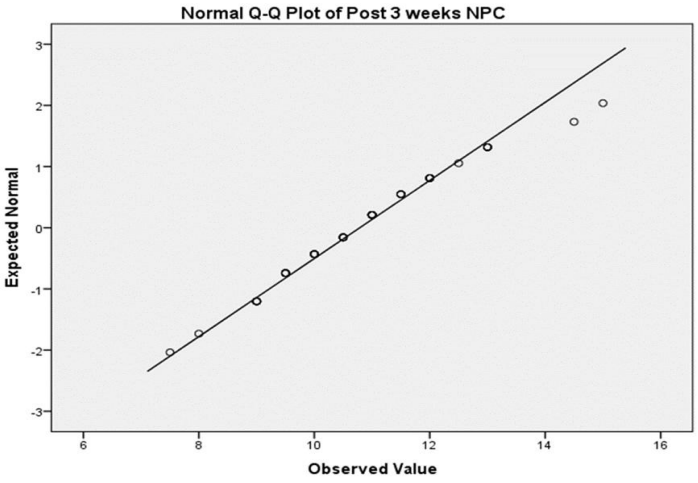

Figure 2. Q-Q plot of 3-week near point of convergence (NPC) measurements.

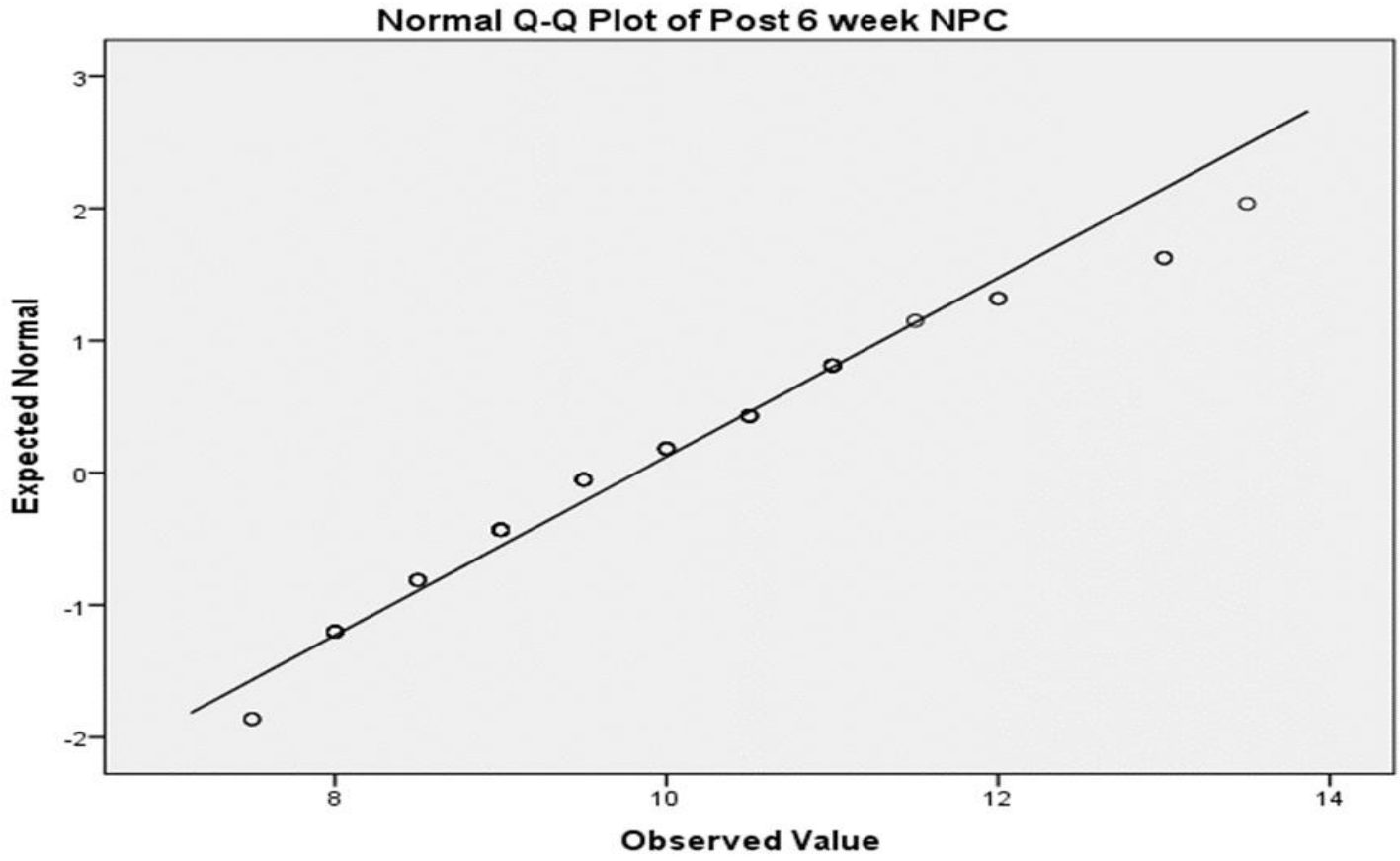

Figure 3. Q-Q plot of 6-week near point of convergence (NPC) measurements.

The findings of this study demonstrated a statistically significant improvement in NPC following six weeks of yogic ocular exercises. The mean NPC reduced from 11.55 cm at baseline to 9.81 cm at the final follow-up, indicating enhanced convergence ability. Statistical analysis using the Friedman and Wilcoxon signed-rank tests confirmed that these improvements were highly significant ($p < 0.001$). Additionally, a reduction in asthenopic symptoms was observed, suggesting that yogic ocular exercises not only improve convergence mechanics but also alleviate functional discomfort associated with convergence insufficiency. These results support the hypothesis that regular activation and relaxation of extraocular muscles through yogic practices may improve muscular tone and coordination, thereby correcting convergence deficits.

The findings of the present study are consistent with previously published literature. Sang-Dol Kim (2016) reported significant improvements in NPC, AC/A ratio, and fusional convergence among nursing students following six weeks of yoga-based eye exercises, highlighting the role of such exercises in reducing ocular fatigue and improving binocular vision parameters (15). Similarly, Kumar and Asif (2017) demonstrated significant improvements in

visual performance measures among school-aged children after six weeks of yoga eye workouts, reinforcing the beneficial role of yogic practices across different age groups (16).

Pandey et al. (2017) further supported the effectiveness of eye exercises by reporting a significant reduction in Convergence Insufficiency Symptom Survey (CISS) scores in children with myopia who performed structured ocular exercises, compared with controls who relied solely on optical correction (17). Although their primary outcome differed, the observed reduction in symptoms aligns with the symptom improvement noted in the current study. Bianchi et al. (2020) also demonstrated short-term improvements in morphoscopic visual acuity following brief yoga eye exercise sessions, suggesting that even short-duration interventions may positively influence visual function (18).

Additional evidence from Gupta and Aparna (2020) showed a significant reduction in eye fatigue severity among students practicing yogic ocular exercises, while fatigue worsened in the control group (19). Muzahid (2020) similarly reported reduced ocular fatigue in school-going children following yogic ocular exercises combined with ergonomic advice during prolonged online learning periods (20). These findings collectively support the role of yogic ocular exercises in relieving visual discomfort and improving ocular efficiency.

Moreover, studies exploring the physiological effects of yogic ocular exercises provide plausible mechanisms for the observed improvements. Sankalp et al. (2017) reported reduced intraocular pressure in glaucoma patients following Trataka-based yogic practices, attributing the effect to improved ciliary muscle function and enhanced aqueous humor outflow (21). Gupta and Aparna (2019) further suggested that yogic ocular exercises increase metabolic activity and intraorbital blood circulation, contributing to improved ocular muscle performance and reduced intraocular pressure (22). These mechanisms may also explain the improved convergence observed in the present study through enhanced extraocular muscle perfusion and coordination.

Overall, the results of this study indicate that yogic ocular exercises are an effective, non-invasive, and low-cost intervention for improving convergence insufficiency and associated symptoms. Given their ease of implementation and minimal risk, these exercises may serve as a valuable adjunct to conventional orthoptic therapy, particularly in young adults.

CONCLUSION

The findings of this study indicate that yogic ocular exercises are effective in improving convergence insufficiency by enhancing the near point of convergence and reducing associated symptoms such as headache, eye strain, and visual discomfort. The observed improvement suggests better coordination and balance of the extraocular muscles involved in near vision tasks. Overall, yogic ocular exercises may serve as a simple, non-invasive, and cost-effective therapeutic approach for the management of convergence insufficiency.

Conflict of Interest

Authors declare no conflict of interest.

Ethical consideration

The study was approved by local research ethics committee.

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Original Article

PHYSICOCHEMICAL ANALYSIS AND COST COMPARISON OF DIFFERENT LOCAL AND MULTINATIONAL BRANDS OF SITAGLIPTIN AVAILABLE IN PAKISTAN

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ABSTRACT:

The main objective of this study was to determine that various generic sitagliptin products from local and multinational brands competing in the local market are pharmaceutical equivalents. A physicochemical comparison was conducted on local and international brands of sitagliptin tablets gathered from local drug outlets of Hyderabad, Pakistan. A total of 5 sitagliptin brands were taken and globally accepted in-vitro tests were performed at Industrial pharmacy laboratory of Department of Pharmaceutics, Faculty of Pharmacy, University of Sindh, Jamshoro Pakistan, during period August 2021 to August 2022. All the sitagliptin products obtained from local market were fulfilling the quality standards required by BP for tests of weight uniformity, diameter, thickness, hardness, friability, disintegration, and World Health Organization (WHO) standards for tests of dissolution and content uniformity/assay. All sitagliptin generics from different local and multinational manufacturing companies are pharmaceutical equivalents and may be prescribed as an alternate to each other.

Keywords: Antidiabetics, Sitagliptin, Quality, Pharmaceutical Equivalents

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder that affects the body's ability to regulate glucose levels. It is characterized by high glucose levels in the bloods caused by either inadequate insulin production or by the reduced body's response towards insulin at receptors (ie insulin resistance). It is mainly classified into two types type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM)(1). The global burden and incidence of diabetes mellitus are high, and it is estimated that the number of people affected will continue to rise. In Pakistan, it was reported that 7 million people confirmed to have DM in 2007, and this count is thought to increase to 14.5 million by 2025(2). The International Diabetes Federation predicts that by 2030, over 643 million people will have diabetes mellitus worldwide(3). Managing type 2 DM involves six classes of oral antidiabetic medications, such as sulfonylureas, meglitinides (Glinides), thiazolidinediones, biguanides, dipeptidyl peptidase IV (DPP-IV) inhibitors, and α-glucosidase inhibitors(4, 5).

Pharmaceutical manufacturer when design a drug, it is marketed under the brand name of the innovator company and protected by intellectual property rights for a period of about 12 years. After this period, Food and Drug Administration (FDA) requires generic brands to carry the active pharmaceutical ingredient (API), doses, dosage form, and its administering mode like the inventor's drug product. Generics must ascertain and show that their brand is equivalent to the original drug product of inventor. Each pharma company's packing and QC areas should meet the equal quality standards to the original product. Generic drugs are typically 80-85% less expensive than their innovator counterparts, making them more affordable for patients. However, this lower price should not come at the expense of quality. Multiple me too formulations increases the likelihood of issues in overall quality(6). Generic medicine brands carry risks bioequivalence results and may also show dissolution profiles, resulting in suboptimal effectiveness in patients(7). Therefore, most medical doctors in Pakistan choose international pharma products, but cost still remains a significant matter to consider. Many prescribers also affirm that prescribing patterns are influenced by pharma companies(8). This research aims to evaluate available brands of Sitagliptin tablets in the local pharmacies. Additionally, the research seeks to identify any low-quality brands. The study was conducted to do a qualitative comparison of OADs of local and international pharmaceutical industries.

METHODS

To determine the quality of sitagliptin by performing physicochemical tests such as test for physical appearance, weight uniformity, thickness and diameter of tablet, disintegration, dissolution and assay. British Pharmacopoeia and WHO criteria for acceptance of quality were used to compare the inferences. Foremost importance was given to all sitagliptin brands that is available in the local market and most frequently used as a treatment. Following were the sitagliptin drug products randomly obtained from the pharma market of Hyderabad, Sindh, Pakistan for the study. Data shown in research is of the drug products obtained and analyzed between August 2021 to July 2022 at Laboratory of Industrial pharmacy situated at Department of Pharmaceutics, University of Sindh, Jamshoro. Sitagliptin brand obtained from drug stores was from Multinational/innovator pharma named as; Sample 01, whereas four generics were of local pharma and coded as; Sample 02, Sample 03, Sample 04 and Sample 05.

Aesthetic test

The appearance of the tablet and existence of any contaminating particles in the drug product were examined by eye. For Tablets having film coat (also known as FCTs), perfectness of coating was also ascertained.

Weight Variation

The weight variation test for the tablets was conducted using a Shimadzu AY220 weighing balance. To perform the test, 20 tablets randomly selected from the commercial pack and individually weighed. Then average weight was taken. The maximum and minimum control limits were then calculated based on the allowed deviation. Only 2 out of 20 tablets were allowed to exceed the permitted range, and no tablet was allowed to exceed twice the allowed limit. Limit was ±10% for tablet weighing ≤80mg, ±7.5% for >80mg and <250 it was, and ±5% for >250mg.

Dimensions

To determine the thickness and diameter of the tablets, a Digital Vernier caliper was used as the equipment. Ten tablet samples were drawn from their blister packs, and the thickness and diameter of each tablet were measured individually. The tablets were placed in the jaws of the Digital caliper, and the obtained deviation from the average thickness of the ten tablets was within ±5%. For tablets, allowed limit was ±5% for diameter up to 12.5mm, while ±3% for diameter above 12.5mm.

Hardness

Not applicable to film coated tablets

Friability

Not applicable to film coated tablets

Disintegration test

USP Disintegration Apparatus was used to test the disintegration time of samples. 6 tablets/brand were drawn for testing. In case disintegration of all the tablets occur in the time specified, results were considered compliant, and if one tablet disintegration time exceeds the allowed limit of time, the test was repeated with 12 more tablets. If 16 out of 18 units completely disintegrated, it shows compliance. Distilled water as the test medium, and a 15minute disintegration time limit for uncoated, 30 minutes for film-coated, and one hour for sugar-coated tablets. The temperature of the medium was controlled at 37°C ±2°C during the test.

Dissolution test

Basket method/USP Dissolution apparatus type I was used for dissolution testing. Dissolution medium used was Water. Both beakers/vessels of dissolution assembly got filled with water to 900ml and maintained to 37°C (±0.5°C). One tablet was inserted to each of baskets and was stroked at 100rpm for 30 minutes. Post 30 minutes, 5ml solution was drawn from each of the two vessels and filtration was carried out through syringe filter 0.45µm. Simultaneously water equivalent to sample drawn was refilled in the vessels. Quantity of Sitagliptin in dissolution medium was then quantified. The acceptable criteria is eight percent of the drug should release within thirty minutes.

Preparation of Standard solution

Standard 10µg/mL solution was prepared by sonicating (10mg) Sitagliptin in 50mL of 0.1N HCl for 10 minutes and then volume made up to 100ml to give 100µg/ml concentration with 0.1N HCl. 1mL of aliquot were poured in 10mL volumetric flask and added with 0.1N HCl to yield 10µg per ml concentration. At the end, drug concentration was quantified by getting absorbance at 268nm. 0.1N HCl was used as blank.

Assay

Perkin Elmer UV/Visible Spectrophotometer ƛ25 was utilized for the content uniformity test. For determination of drug samples, 20 tablets were taken of each brand and was weighed and powdered. The powdered drug equal to

100mg Sitagliptin was taken in 100mL flask already containing 50mL 0.1N HCl. The mixture was then homogenized using sonicator for 15 minutes. Final volume was made using 0.1N HCl to 100µg/mL. At the end it was clarified via (0.45µm) disc filter. 1ml filtrate then transferred by A-grade pipettes in 10mL flasks. Final volume of the solutions were made with 0.1N HCl to produce concentration of 10µg/mL. The produce sample solution was then quantified for the sitagliptin(9). The process is summarized in Figure 1.

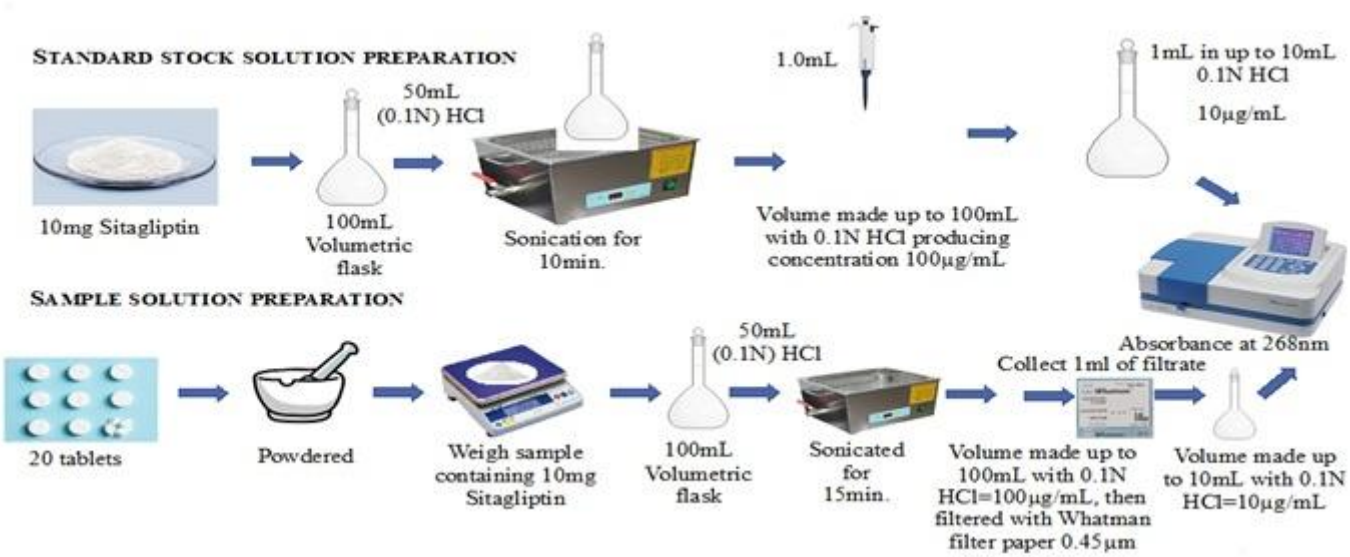


Figure 1. Protocol of Assay of Sitagliptin

Statistical methods

Statistical analysis was performed using statistical package for social science (SPSS) version 20.0. All the categorical variables were presented as frequencies and percentages.

RESULTS

The collected samples of sitagliptin were within their mentioned expiry date. The aesthetic test revealed that the dosage forms were in perfect condition, showing no signs of damage or cracks. The surface appeared smooth, and there were no visible contaminants present. During the test for weight variation, all twenty tablets demonstrated compliance with the allowed 5% limit in weight as specified in the test. Additionally, in the dimension assessment, all 10 tablets met the specified limits, with an allowed variation of 5%. For more detailed observations of weight variation and tablet dimensions, a summary is given in Table1.

During the test for disintegration, all 6 tablets eroded within half hour. Table 2 presents the average disintegration time. Dissolution test also showed compliance as mentioned in Table 2. Assay result also showed that drug products of all brands were within their specified limits. The results of the assay can be found in Table 2 and Figure 2.

Table 1. Results of weight uniformity and thickness and diameter of the tablets

Sample	Average Weight (mg)	SD	Allowed limit (±5%)	UCL	LCL	No. of samples complied
Weight variation						
Sample-01 (International)	413.73	±2.929	20.69	434.42	393.04	20/20
Sample-02 (Local)	394.93	±2.125	19.75	414.68	375.18	20/20
Sample-03 (Local)	306.89	±1.072	15.34	322.23	291.54	20/20
Sample-04 (Local)	434.68	±3.431	21.73	456.41	412.94	20/20
Sample-05 (Local)	325.92	±4.253	16.30	342.22	309.63	20/20
Thickness						
Sample-01 (International)	4.42	±0.035	0.22	4.64	4.20	10/10
Sample-02 (Local)	5.02	±0.048	0.25	5.27	4.77	10/10
Sample-03 (Local)	3.66	±0.043	0.18	3.84	3.48	10/10
Sample-04 (Local)	4.84	±0.060	0.24	5.08	4.60	10/10
Sample-05 (Local)	3.56	±0.077	0.18	3.74	3.38	10/10

Diameter						
Sample-01 (International)	10.02	±0.033	0.50	10.52	9.52	10/10
Sample-02 (Local)	9.07	±0.048	0.45	9.52	8.62	10/10
Sample-03 (Local)	10.13	±0.036	0.51	10.64	9.62	10/10
Sample-04 (Local)	10.17	±0.060	0.51	10.68	9.66	10/10
Sample-05 (Local)	9.90	±0.064	0.49	10.39	9.40	10/10

* SD=Standard Deviation, UCL=Upper Control Limit, LCL-Lower Control Limit

Table 2. Results (hardness, friability, disintegration, dissolution and assay test)

Sample	Average Hardness and Friability	Disintegration Test	Dissolution test (30 minutes)	Assay	Cost comparison of Local vs Multinational brands
Sample 01	N/A	8 minutes and 52.3 seconds	83%	102.19%	Local brands were 58-66% economical than multinational brands
Sample 02		7 minutes and 56.8 seconds	87%	97.33%	
Sample 03		9 minutes and 22.5 seconds	82%	92.80%	
Sample 04		9 minutes and 35 seconds	88%	101.14%	
Sample 05		7 minutes and 44.6 seconds	86%	96.10%	

DISCUSSION

The effectiveness of medications in treating patients depends on the quality and amount of the API contained in the drug product. To ensure that the medications meet the required standards, conventional quality assessment involves an examination and measurement approach in quality control. This process ensures that the medications adhere to predetermined standards of quality. Quality is essentially the degree to which a particular substance conforms to a reference or standard. In the context of pharmaceutical manufacturing and quality assurance, the concept of quality has significantly evolved from a narrow perspective. Presently, the accepted definition of quality emphasizes "fitness for purpose," indicating that the focus is on ensuring the product's suitability for its intended use(10).

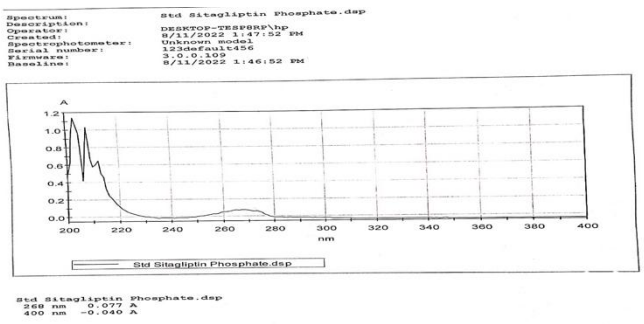
This research aimed to assess the quality of various products of sitagliptin. The findings concerning appearance and dimensions fell within the acceptable limits, aligning with the results of previous research done on sitgliptin in Pakistan and Yemen(11, 12). Nebal and Haider in 2014 in a study showed Sitagliptin generic products quality against Innovator's Sitagliptin. Hence, 5 different products were taken from Middle East drug stores. The physicochemical tests' results were juxtaposed to specifications laid down by USP31.Finally proved that generic brands were equivalent to innovator(12).

Moreover, in a study conducted by Tarkase, K., et. al. (2014) on sitagliptin tablets shown that the method developed for qualitative and quantitative assessment of sitagliptin was effective for cheaper analysis of sitagliptin brands and estimation of sitagliptin in its supplied form was efficiently done. Hence, with these assay test methods, the brands tested in this study also complied to allowed limits of content uniformity test(9).

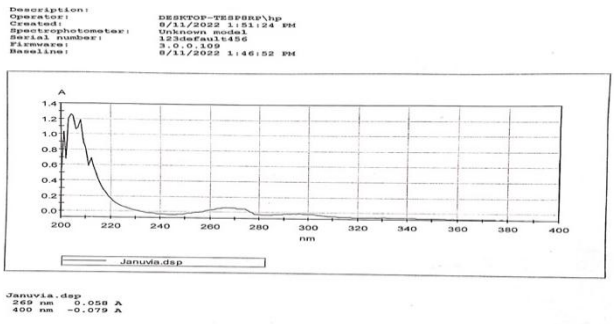
Additionally, it was shown that sitagliptin is a very efficient medicine in the control of diabetes mellitus type II, hence the quality equivalency shown in this study between generic and innovator brands conforms that local brands are expected to work as innovator brand(13).

WHO require drug products to contain 95-105 percent of the drug entity in the medication at the time of release of product from the manufacturers' site, and once it reaches commercial shelves should at least contain 90-110% of the active chemical entity, hence this study concluded with the results which were in consonance with the guidelines proposed by the WHO and the local and international brands were therapeutically comparable(14).

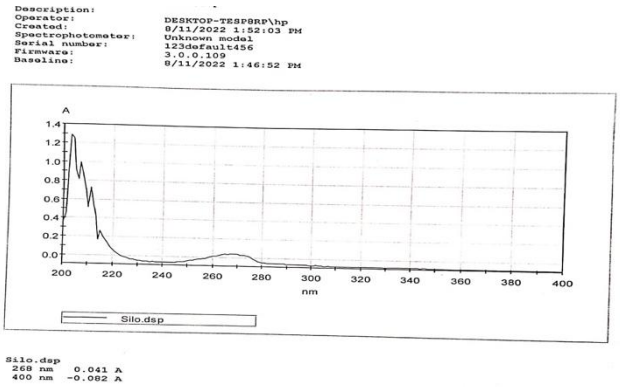
ASSAY SPECTRUMS



Standard



Sample 1



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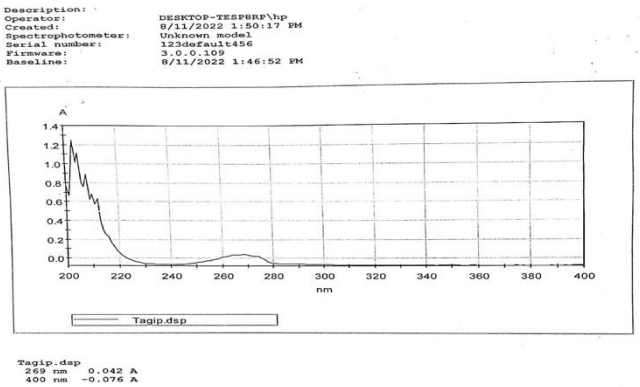

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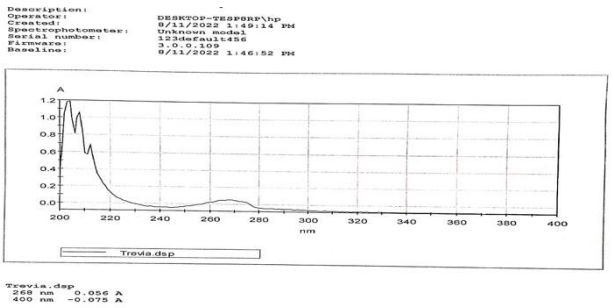
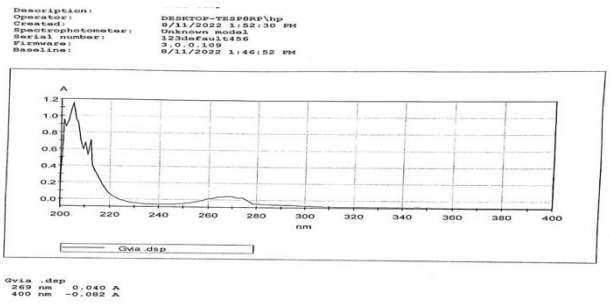


Sample 4



Sample 5

Figure 2: Spectrogram of Assay of 5 brands of Sitagliptin along with standard

CONCLUSION

All the sitagliptin samples collected from the local market were complying with the standards given in British pharmacopoeia and WHO at the very moment when selected for weight uniformity, thickness, diameter test, disintegration, dissolution and assay were conducted. In this study, no substandard or counterfeit brand emerged. The medicinal products from local and multinational brands may be regarded as pharmaceutical equivalents and can be prescribed as an alternate choice to each other.

Conflict of Interest

Authors declare no conflict of interest.

Ethical consideration

The study involved only laboratory testing of oral antidiabetics and did not required approval of research ethics committee as no animal/human subjects or their data was used.

Acknowledgement

Thanks to all my friends and colleagues who helped me in my study. Special thanks to my supervisors Dr. Imran Suheryani, Prof. Dr. Muhammad Ali Ghoto and my mentor 'Prof. Dr.Ubed-ur-Rehman Mughal' Chairman of Department of Pharmaceutics, Faculty of Pharmacy, University of Sindh, Jamshoro.

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Original Article

NO SIGNIFICANT ASSOCIATION BETWEEN 40BP INS/DEL PROMOTER POLYMORPHISM OF MDM2 AND BREAST CANCER SUSCEPTIBILITY IN PAKISTANI WOMEN

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ABSTRACT:

Breast cancer remains the most prevalent malignancy among women, and is the second leading cause of mortality worldwide. Genetic heterogeneity in the MDM2 promoter region has been associated with increased cancer susceptibility. The study was designed to assess the impact of a 40-bp deletion/insertion mutation of the MDM2 gene (at position 1518, which has a putative TATA pattern) in both breast cancer patients and healthy participants. A total of 200 female participants were included in the present study, comprising 100 histologically confirmed breast cancer patients and 100 age- and sex-matched healthy controls. Patient samples were obtained from Bolan Medical Complex (BMC) and the Center for Nuclear Medicine and Radiotherapy (CENAR), Quetta, Pakistan. Along with blood sample collection, information regarding demographic, reproductive, and clinical characteristics was recorded. Genotyping of the MDM2 gene 40-bp insertion/deletion (ins/del) polymorphism was carried out using specific forward and reverse oligonucleotide primers. The genotype frequencies of the MDM2 polymorphism among breast cancer patients were 57% for ins/ins, 36% for ins/del, and 7% for del/del, whereas in the control group they were 59%, 35%, and 6%, respectively. The calculated odds ratio for the deletion allele was 1.208, with a 95% CI ranging from 0.383 to 3.812 ($p = 0.939$). No statistically significant associations were observed between breast cancer and menopausal status, age at menopause, parity, number of children, use of oral contraceptives, or history of breastfeeding ($p > 0.05$). These results suggest that the 40-bp ins/del polymorphism in the promoter region of the MDM2 gene is not significantly associated with the development of breast cancer in the studied population.

Keywords: Breast cancer, insertion/deletion polymorphism, MDM2, Oligonucleotide primers, Menopause, breastfeeding

INTRODUCTION

Breast cancer (BC) is a term used to describe the abnormal growth and multiplication of cells originating from breast tissue. A breast tumor is a serious and common disease that affects women's health and is one of the leading causes of cancer-related death. According to a study, 23% of all cancer patients are diagnosed with breast cancer, which also accounts for 14% of cancer-related deaths. Breast cancer affects women 100 times more often than men. Although men are less likely to develop breast cancer, they can still be affected. Different ethnic groups have varying rates of cancer incidence (1). Breast cancer is classified into distinct categories based on its stage, aggressiveness, and genetic composition. Advancing age, female gender, nulliparity, less breastfeeding, heredity, increased hormone levels, and individual lifestyle are the key risk factors linked with the development of breast cancer. Although the cause of breast cancer is uncertain, genetic factors have been demonstrated to have a significant influence on its pathogenesis and progression (2). Among genetic changes, the tumor suppressor protein p53 (tumor suppressor protein) is the main governing factor in a variety of cell lines (3).

In most multicellular organisms, it plays an important function in cancer suppression. It protects genes against mutation and plays a role in maintaining stability. It promotes a transcriptional pathway that induces apoptosis, cell cycle arrest, and autophagy, among other cellular damages, in response to genotoxic stress and oncogenic signals (3). Overexpression of MDM2, a cellular antagonist, can inhibit p53 action in some situations. MDM2 is a key component of the p53 pathway. MDM2 is a p53-specific E3 ubiquitin enzyme that promotes proteasome degradation of p53. MDM2 was discovered to be one of three genes (MDM1, MDM2, and MDM3). This gene was identified on an extrachromosomal acentromeric nuclear region (4). The human MDM2 gene has 11 exons, two promoter regions, and a p53 intronic promoter. It is situated on chromosome 12q14.3–q15.1 (5), present on the q-arm. MDM2

expression may be affected by genetic changes within either of the promoters. MDM2 regulates p53 activity in a variety of ways, and even small changes in MDM2 levels can have an impact on the p53 pathway. MDM2 binds directly to the transactivation domain of p53, which decreases p53 transcriptional activity. Second, it acts as an E3 ubiquitin ligase, facilitating p53 ubiquitination and degradation. Finally, it attaches to p53 inside the nucleus and transports it to the cytoplasm, causing it to degrade (6).

MDM2 is a 40-bp Ins/Del mutation with a putative TATA motif in the promoter region, one of the most studied polymorphisms (7, 8). Because of MDM2's tumorigenic role, researchers may presume that people who have the 40bp deletion allele have an increased chance of developing breast cancer during their lifespan (9). However, there is limited data available from Pakistani population thus this study was conducted.

METHODS

A total of 200 women participated, including 100 patients diagnosed with breast cancer, along with 100 healthy women with no history of cancer as a control group, having the same age range. After obtaining informed consent, all the participants were recruited from CENAR and Bolan Medical Complex (BMC) hospitals Quetta, Pakistan.

Assessment of Demographic and Reproductive Factor

Several demographic and reproductive factors relevant to breast cancer, such as age, ethnicity, gender, smoking status, marital status, family history, menopause and menarche, number of children, nulliparity, breastfeeding, age at first childbirth, age at cancer diagnosis, and other factors, were assessed through interviews and structured questionnaires. Under strict aseptic conditions, 5 ml of blood was drawn from each participant for DNA extraction and subsequent mutational analysis.

DNA Extraction

Genomic DNA was extracted from whole blood samples collected in EDTA tubes employing the standard Phenol-Chloroform method. The extracted DNA was diluted with TE buffer, and its purity was checked using a NanoDrop spectrophotometer, and quantified using a 0.8% agarose gel. The extracted DNA was stored at -20°C for future analysis.

Polymerase Chain Reaction (PCR)

PCR was carried out for amplification of the MDM2 gene promoter region, associated with breast cancer mutations. Gene-specific primers, both forward (5`-GACCACTATGTTTAAGGAAG-3`) and reverse (5`-TGACTCACCTACTTTCCCAC-3`), were employed, producing fragments of 287 bp and 247 bp for the ins allele and del allele, respectively. The 25µl reaction mixture contained 2 µl of genomic DNA, 2.5 µl of dNTPs, 2.5 µl of MgCl2, 1 µl of each primer, 0.3 µl of Taq DNA polymerase, and 2.5 µl of PCR buffer. Amplification was achieved under standard PCR conditions, and the resulting PCR products were analyzed by 1.5% agarose gel electrophoresis and visualized under UV light.

Statistical Methods

Statistical analyses were carried out using Statistical Package for Social Sciences (SPSS), with categorical variables expressed as frequencies and percentages. The association of demographic as well as reproductive factors with breast cancer risk was evaluated by chi-square tests, and a p-value ($p<0.05$) was considered statistically significant.

RESULTS

Genotypic Distribution of MDM2 40-bp Insertion/Deletion (I/D) Polymorphism

To assess the correlation between the 40-bp I/D polymorphism in the MDM2 gene and breast cancer susceptibility, genotypic distribution was analyzed in 100 breast cancer patients and 100 age- and sex-matched healthy controls. The genotype and allele frequencies, along with the corresponding odds ratios (OR) and 95% confidence intervals (CI), are summarized in Table 1. No significant difference in genotype distribution was observed between patients and controls. The deletion allele showed no significant association with breast cancer risk ($p = 0.726$, OR = 1.085; 95% CI: 0.687–1.715). Similarly, co-dominant, dominant, and recessive genetic models did not reveal any statistically significant association between the polymorphism and disease occurrence.

Demographic and Clinical Characteristics

Demographic characteristics of patients and their association with the 40-bp I/D polymorphism are presented in Table 2. No significant association was found between age and genotype distribution ($p = 0.647$).

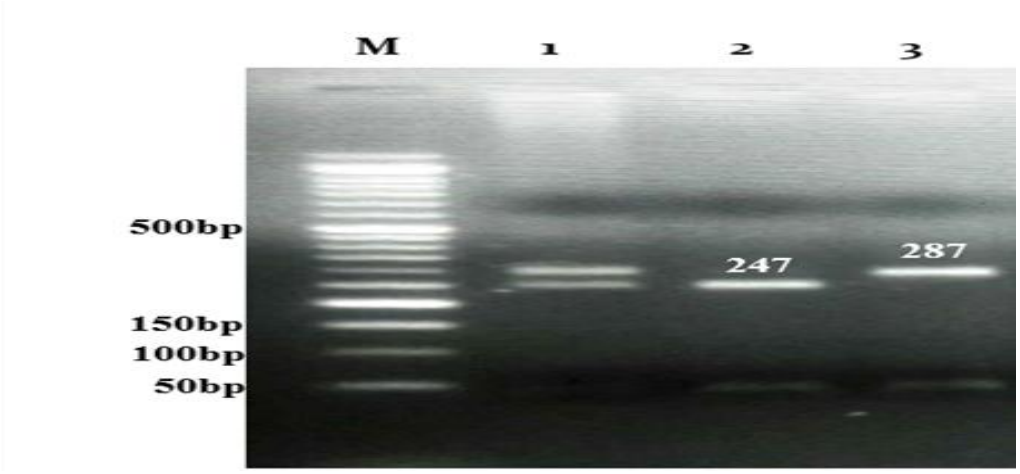

Figure 1: Gel image of the PCR product of the 40-bp I/D polymorphism of MDM2. Well 1: 50 bp DNA marker; Well 2, heterozygote; Well 3, deletion; Wells 4, insertion

Table 1. Distribution of allele frequencies of the 40bp I/D mutation

40bp ins/del	Patients (%)	Control (%)	Co-dominant	P-value
Co-dominant				
Ins/ins	57	59	1	
Ins/del	36	35	1.065(0.590-1.922)	0.939
Del/del	7	6	1.208(0.386-3.812)	
Dominant				
Del/del	7	6	1	
Del/Ins +Ins/Ins	93	94	0.848(0.275-2.619)	0.774
Recessive				
Del/Del + Ins/Del	44	42	1	
Ins/ins	56	58	1.085(0.620-1.900)	0.775
Allele				
Ins	150	153	1	
Del	50	47	1.085(0.687-1.715)	0.726

Among the patients, 96% were married, and 92% had given birth. Approximately 15% of patients reported having their first pregnancy before the age of 25 years, and 88% had a history of breastfeeding. Early menarche (≤12 years) and late menopause (≥50 years) were reported in 67% and 8% of cases, respectively. The use of oral contraceptive pills was noted in 60% of participants, while 85% were non-smokers. Family history of breast cancer was positive in 8% of patients. In total, 42% of women were premenopausal, while 58% were postmenopausal. Menstrual status did not show any significant correlation with the presence of the polymorphism. No significant associations were observed between breast cancer occurrence and family history, smoking status, or inheritance pattern.

Table 2. Association of 40-bp I/D polymorphisms with demographic information

Variables	Genotype			Chi value	P-value
Age	Del	Ins	Ins/Del		
21-40	8(7%)	60(52.6%)	46(40.4%)	2.485	0.647
41-60	2(2.7%)	40(54.1%)	32(43.2%)		
61-80	2(16.7%)	4(33.3%)	6(50.0%)		
Ethnicity					
Baloch	0(0%)	32(53.3%)	28(46.7%)	6.189	0.402
Pathan	4(5.8%)	54(51.9%)	44(42.3%)		
Persian	4(18.2%)	12(54.5%)	6(27.3%)		
Punjabi	2(14.3%)	6(42.9%)	6(42.9%)		
Smoking status					
No	12(7.3%)	82(50%)	70(42.7%)	1.718	0.424
Yes	0(0%)	22(61.1%)	14(38.9%)		
Inheritance					
From mother	0(0%)	6(75%)	2(25%)	0.961	0.619
None	12(6.2%)	98(51.0%)	82(42.7%)		

Hormonal and Reproductive Factors

The relationship between the 40-bp I/D polymorphism and hormonal or reproductive characteristics is summarized in Table 3. No significant association was observed between the polymorphism and age at menarche, menopausal age, number of children, breastfeeding status, or oral contraceptive use. Additionally, radiation exposure showed

a borderline association (p = 0.051), although it did not reach statistical significance. Overall, the 40-bp I/D polymorphism in MDM2 did not show a statistically significant association with breast cancer risk or with demographic, reproductive, or hormonal factors in the studied population.

Table 3. Association between 40-bp I/D mutation with hormonal factors in case and control.

Variable	Del	Ins	Ins/del	Chi value	P value
Menarche(Years)					
11	0(0%)	4(50.0%)	4(50.0%)	3.048	0.931
12	10(8.2%)	64(52.5%)	48(39.3%)		
13	2(3.8%)	24(46.2%)	26(50.0%)		
14	0(0%)	10(71.4%)	4(28.6%)		
15	0(0%)	2(50.0%)	2(50.0%)		
Menopause age					
No menopause	6(4.8%)	70(55.6%)	50(39.7%)	3.093	0.797
30-39	2(11.1%)	6(33.3%)	10(55.6%)		
40-49	4(9.1%)	20(45.5%)	20(45.5%)		
50-59	0(0%)	8(66.7%)	4(33.3%)		
Number of children					
0-4	8(7.5%)	58(54.7%)	40(37.7%)	1.515	0.824
5-9	4(5.4%)	36(48.6%)	34(45.9%)		
10-14	0(0%)	10(50.0%)			
Breastfeeding					
No	0(0%)	18(52.9%)	16(47.1%)	1.357	0.507
Yes	12(7.2%)	86(51.8%)	68(41.0%)		
Oral contraception					
No	8(5.5%)	78(53.4%)	60(41.1%)	0.280	0.869
Yes	4(7.4%)	26(48.1%)	24(44.4%)		
Radio exposure					
No	2(3.3%)	56(45.9%)	62(50.8%)	5.946	0.051
Yes	8(10.3%)	48(61.5%)	22(28.2%)		

DISCUSSION

Globally, among all types of cancer cases, the contribution of BC is 23% (11). Breast cancer starts from breast tissue, most commonly from the inner lining of ducts (ductal carcinoma) or the lobules (lobular carcinoma)(12). Hazard variables for breast cancer may be hereditary qualities, the need for childbearing or need of breast bolstering, increase the amount of few hormones. For breast carcinoma, female gender and increase of age are the important risk factors. Alter in dietary habits, exposure to light contamination, tobacco, high intake of fats, use of liquor also increase risk of development of breast cancer (13). Early menarche, menopause at a late age, first pregnancy at a late age, being pregnant at least three times and the presence of this cancer within first degree relatives are some factors that increased the hazards of BC. A strong association of breast cancer risk with increased age of menopause was observed in many studies (14).

The present study investigated the potential influence of the MDM2 40-bp insertion/deletion (I/D) polymorphism on the risk of developing breast cancer. The findings demonstrated no significant association between this genetic variant and breast cancer susceptibility in the studied population. In contrast, research conducted among Iranian women reported that the MDM2 40-bp I/D polymorphism was linked to an increased risk of breast cancer (2). Similarly, studies involving Chinese cohorts have revealed a significant correlation between this polymorphism and the development of lung cancer (9) as well as hepatocellular carcinoma(15). However, other investigations carried out within Chinese populations found no relationship between the MDM2 40-bp I/D variant and breast cancer risk (8). The MDM2 is linked with p53 and bcl2 pathway that repairs the damaged DNA and also relates to the initiation of apoptosis in case of failure to DNA repair. The MDM2 actually degardes p53 protein once its function is over. In this study when there is no apparent association of MDM2 found in the study population could be linked with a single gene study as this works in a pathway, thus other genes and also epigenetics have its role to play. Therefore it is considered as a limitation of the study. The clinical outcome was not evaluated in this study, though MDM2 might have strong link with it. It is also considered as a limitation. However, the large sample size from a single centre with standard protocols for evaluation of MDM2 susciptability is considered as strength of the study.

CONCLUSION

In the Pakistani female population low levels of conventional risk factors are observed since they show high fertility, numerous births, expanded period of nourishing their child, and early age pregnancy. The MDM2 did not show significant association with breast cancer susceptibility in studied population. Large scale cohort studies with inclusion of other related genes of p53 pathway are recommended.

Conflict of Interest

Authors declare no conflict of interest.

Ethical consideration

The study was approved by local research ethics committee.

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Short review

EXPLORING THE ASSOCIATION BETWEEN PSYCHOLOGICAL DISTRESS AND CANNABIS EDIBLE USE AMONG U.S. ADULTS: A SHORT REVIEW

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ABSTRACT:

Cannabis edibles have become increasingly popular in the United States (U.S), however, limited research has explored their relationship with mental health. This study examined whether adults experiencing past-month psychological distress were more likely to use cannabis edibles compared with those without distress. Data were drawn from the 2023 National Survey on Drug Use and Health (NSDUH). Adults aged ≥ 18 years were included. Past-month cannabis edible use (IRMJMONEAT) was the dependent variable, and past-month psychological distress (SPDPSTMON) was the primary predictor variable. Weighted prevalence estimates and survey-weighted logistic regression models were applied, adjusting for relevant sociodemographic and behavioral factors. The Weighted prevalence of edible use was 5.6% (95% CI 5.2–5.9) among adults without distress and 13.5% (95% CI 12–15) among those with distress. In the adjusted regression models, psychological distress was significantly associated with edible use (AOR = 1.44, 95% CI 1.21–1.71, $p < 0.001$). In conclusion the psychological distress was independently associated with hight cannabis edible use among U.S. adults. These findings underscore the importance of integrating mental-health screening and harm-reduction strategies into cannabis prevention and treatment frameworks.

Keywords: Psychological distress, cannabis edibles, substance use, mental health

INTRODUCTION

Cannabis legalization across the United States has contributed to the growing availability and acceptance of alternative cannabis products, including edibles such as gummies, chocolates, and beverages. These products are often perceived as more discreet and potentially safer alternatives to smoking or vaping, attracting both novice and regular consumers (1,2,3). However, the pharmacological characteristics of edibles differ markedly: oral ingestion leads to delayed onset and prolonged duration of psychoactive effects, increasing the likelihood of accidental overconsumption, anxiety, and impaired judgment (4,5).

Psychological distress—comprising symptoms of anxiety, depression, and emotional suffering—has been consistently associated with higher cannabis use and misuse (6,8). Individuals experiencing distress often report using cannabis for self-medication or to manage psychological symptoms (9,10). Yet, frequent or high-potency cannabis consumption may exacerbate anxiety and depressive symptoms, suggesting a potential bidirectional relationship between cannabis use and mental health (12,13). Opioid and other drug use can further intensify mental health challenges and often overlaps with cannabis behaviors, including marijuana edible consumption. National data show that approximately 48% of individuals with opioid use disorder experience co-occurring depression or anxiety, and nearly 32% report serious psychological distress or suicidal ideation (7,14). Among people engaging in polysubstance use involving opioids, alcohol, and cannabis, the prevalence of depressive symptoms rises to over 55%, and anxiety disorders exceed 40%, compared with less than 15% among non-users. Marijuana edibles, often perceived as safer alternatives, are increasingly used for emotional regulation or relief of withdrawal symptoms, yet their delayed onset and prolonged psychoactive duration frequently lead to overconsumption, panic, or mood destabilization. Evidence suggests that individuals with prior opioid or stimulant use are two to three times more likely to consume high-potency cannabis products or edibles, heightening risks of paranoia, cognitive decline, and depressive relapse (8,11). This convergence of substance uses and psychological distress illustrates a reinforcing, cycle in which self-medication perpetuates emotional dysregulation, underscoring the urgent need for integrated, dual-diagnosis prevention and treatment strategies.

Despite these findings, limited research has explored how psychological distress relates specifically to cannabis edible use, a distinct consumption method with unique pharmacological risk and behavioral patterns. This study aims to assess the association between past-month psychological distress and cannabis edible use among U.S. adults using 2023 NSDUH data. It was hypothesized that adults with psychological distress would have significantly greater odds of edible use compared with those without distress.

METHODS

This cross-sectional study utilized data from the 2023 National Survey on Drug Use and Health (NSDUH), conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA). The NSDUH employs a multistage, stratified probability sampling design to represent the civilian, noninstitutionalized population of the United States aged ≥ 12 years. Data collection was performed using computer-assisted personal human-subject review because the data are fully de-identified. The analytic sample was restricted to adults aged ≥ 18 years (CATAG3 ≠ 1). Participants were included if they provided valid responses for both variables: psychological distress (SPDPSTMON) and cannabis edible use (IRMJMONEAT). Cases with missing, incomplete, or invalid responses were excluded from the analysis. Sampling weights, strata, and primary sampling units (PSU) were applied to produce nationally representative estimates.

The dependent variable in this study was *past-month cannabis edible use*, assessed using the NSDUH item *IRMJMONEAT*, which asked respondents whether they had consumed cannabis-infused food products or beverages during the past 30 days. Responses were dichotomized as 1 = yes and 0 = no.

The primary independent variable was *past-month psychological distress*, measured using the *SPDPSTMON* item derived from the six-item Kessler Psychological Distress Scale (K6). Respondents reporting moderate-to-severe psychological distress during the past 30 days were coded as 1 (yes), while those reporting no psychological distress were coded as 0 (no).

Covariates included a range of sociodemographic and behavioral characteristics previously associated with cannabis use. These comprised age group, gender, race/ethnicity, sexual identity, educational attainment, annual household income, and metropolitan residence status. Policy-related and behavioral factors were also considered, including state-level medical marijuana law (MML) status, *past-month tobacco use*, and *past-month alcohol use*. All variables followed the definitions provided in the NSDUH public-use codebook to ensure comparability with prior national analyses. Survey design variables (weights = ANALWT2_C, strata = VESTR_C, and PSUs = VEREP) were incorporated using the survey and srvyr packages in R (version 4.3.3). Weighted prevalence estimates were calculated using svyby(), and survey-weighted logistic regression models were performed using (svyglm() to estimate adjusted odd ratios (AORs) and 95% confidence intervals (CIs). A p-value of < 0.05 was considered statistically significant.

RESULTS

Among U.S. adults aged ≥ 18 years, the weighted prevalence of past-month cannabis edible use was 5.6% (95% CI 5.2–5.9) among those without psychological distress and 13.5% (95% CI 12–15) among those with distress (Figure 1). This represents a more than twofold difference in prevalence between groups. Adults experiencing psychological distress were significantly more likely to have used cannabis edibles within the past month, suggesting a meaningful association between emotional suffering and non-inhaled cannabis use.

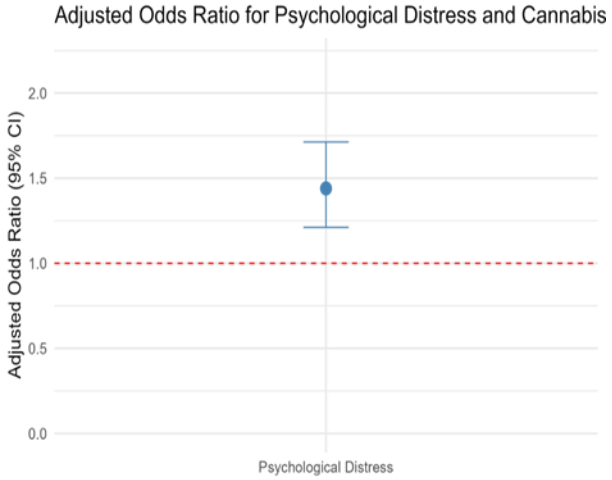

Figure 1. The adjusted odds ratio for the association between psychological distress and past-month cannabis edible use among U.S. adults. The plot shows that individuals experiencing psychological distress had significantly higher odds of consuming cannabis edibles (AOR = 1.44, 95% CI: 1.21–1.71) compared to those without distress. The confidence interval lies entirely above the null value of 1.0, indicating a statistically significant and positive relationship. This finding reinforces that psychological distress is an independent and consistent predictor of cannabis edible use, even after adjusting for demographic, behavioral, and policy-level covariates.

When examined across sociodemographic categories, edible use was highest among young adults aged 18–34 years and progressively declined with age. Women demonstrated slightly higher rates of edible use than men, while sexual-minority adults exhibited disproportionately higher prevalence compared with heterosexual adults. Edible use was also more common among individuals with some college education and those living in metropolitan areas. Additionally, respondents from states with medical marijuana laws (MMLs) reported higher use, reflecting greater product accessibility and social acceptance.

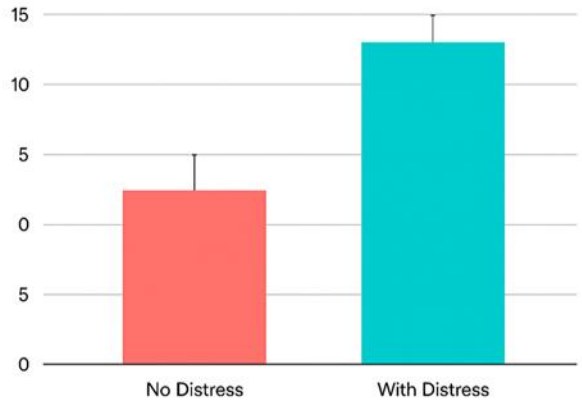

Figure 2. Weighted prevalence f past-month cannabis edible use by psychological distress among U.S. adults (NSDUH 2023)

Figure 2. The weighted prevalence of past-month cannabis edible use among U.S. adults, comparing individuals with and without psychological distress based on 2023 NSDUH data. The results show a marked difference between groups—those without distress reported an edible use rate of approximately 5.6%, while individuals experiencing psychological distress reported a substantially higher rate of 13.5%. The error bars reflect narrow confidence intervals, indicating reliable national estimates. This clear visual pattern demonstrates that adults facing psychological distress are more than twice as likely to consume cannabis edibles, underscoring a strong association between emotional distress and non-inhaled cannabis behaviours. Behavioural analysis revealed that tobacco users were nearly three times more likely and alcohol users twice as likely to consume edibles compared to non-users. Furthermore, individuals who had received mental-health treatment or support in the past year reported higher edible use, suggesting overlap between psychological-care engagement and substance use.

DISCUSSION

This nationally representative analysis demonstrates that adults experiencing psychological distress have significantly higher odds of cannabis edible use compared with those without distress. The strength of the association remained significant even after adjusting for demographic, behavioural, and policy-related variables, suggesting that psychological distress plays a substantial role in shaping cannabis-use behaviours. These findings extend the existing literature linking psychological distress with general cannabis use [12,13] by specifically examining edible consumption, a modality that has becoming increasingly prevalent in legalized cannabis markets. Several behavioral and psychological mechanisms may explain this association. Individuals experiencing psychological distress may perceive edibles as a safer and less stigmatizing option for self-managing symptoms of anxiety or depression. The delayed onset and prolonged psychoactive duration of edibles may create a perception of sustained symptom relief. However, these same characteristics can also increase the risk of overconsumption and dysphoric experiences, such as anxiety, depersonalization, or paranoia which may potentially exacerbate mental health symptoms among vulnerable individuals (5,8).In addition, inconsistent product labeling and variability in THC concentrations further complicate dosage control and increase the likelihood of unintended psychoactive effects.

The sociodemographic differences observed in this study, particularly higher prevalence of edible use among younger adults, women, and sexual minorities, are consistent with previously reported national trends in cannabis use and mental health disparities (8,9,10). These populations often face greater psychosocial stressors and may be more frequently exposed to social environment where cannabis products are normalized. During the COVID-19 pandemic, evidence indicate that global rates of mental health problems and substance use increased substantially, with anxiety and depressive symptoms nearly tripling to affect about 30–35% of adults, compared with pre-pandemic levels below 10%. Concurrently, alcohol and drug use increased by approximately 25–30%, and nearly one in four adults reported heavier or more frequent consumption as a coping mechanism for stress, isolation, or financial strain (17). These findings highlight how pandemic-related disruptions amplified psychological distress and reinforced substance-use behaviors, thereby contributing to a sustained public health burden. The positive association between edible use and residence in states with medical marijuana law (MML) further underscores the influence of policy environments on behavioral health, as legalization broadens access and shapes public perceptions of safety and risk (18,19).

The strong association observed between edible use, concurrent alcohol and tobacco suggests polysubstance behavior patterns, reinforcing the need for integrated prevention and treatment approaches that address multiple

substances and underlying psychological conditions simultaneously (15,16). Routine screening for psychological distress among cannabis users could allow clinicians to identify individuals at higher risk for dependence or adverse reactions, improving early intervention strategies. Moreover, individuals living with HIV frequently face intersecting challenges of substance use and partner violence, with studies showing that up to 35–40% report drug or alcohol misuse and nearly one in three experience intimate partner violence, both of which substantially heighten psychological distress and increase vulnerability to marijuana and other substance use (20,21).

Several limitations of this study should be acknowledged, the cross-sectional design, which limits causal inference, reliance on self-report data, and the absence of detailed metrics on THC dosage, frequency of use, or medical versus recreational intent. Future research should employ longitudinal designs to establish temporal directionality, explore neurobiological mechanisms linking distress and edible use, and examine the role of marketing, accessibility, and product diversity in shaping use patterns and mental-health outcomes.

Despite these limitations, the results carry significant public health and policy implications. As cannabis edibles continue to expand in availability, potency, and consumer appeal, public health campaigns should prioritize evidence-based education on delayed onset, safe dosing practices, and potential psychological and cognitive risks associated with high-THC formulations (22,23). Policymakers should prioritize labeling accuracy, potency regulation, and consumer education to minimize unintended consequences among vulnerable populations.

CONCLUSION

Psychological distress is independently associated with ab increased likelihood of past-month cannabis edible use among U.S. adults. As edible products become more potent and accessible, mental-health and substance-use frameworks must evolve to address the intersection between emotional distress and cannabis-use behaviors. Integrating mental-health screening, counselling, and harm-reduction education into public-health and clinical settings is essential. Future studies should further investigate causal pathways, product characteristics, and the influence of cannabis policy on psychological well-being.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

Public-use NSDUH data are freely available from the Substance Abuse and Mental Health Services Administration (SAMHSA): https://www.samhsa.gov/data/

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