WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 3, 1734-1759. Review Article ISSN 2277–7105

A REVIEW ON NANOTECHNOLOGY AS SUPERIOR ALTERNATIVE FOR TARGETED THERAPY IN SKIN CANCER

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Article Received on 05 Jan. 2026,
Article Revised on 25 Jan. 2026,
Article Published on 04 Feb. 2026,

https://doi.org/10.5281/zenodo.18481131

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How to cite this Article: Shaikh Suhel Rahimoddin[1]*, Mr. Shikare S. H.[2], Dr. Ganesh S. Tolsarwad[3] (2026). A Review on Nanotechnology as Superior Alternative For Targeted Therapy in Skin Cancer. World Journal of Pharmaceutical Research, 15(3), 1734–1759.

1. ABSTRACT

Skin cancer remains one of the fastest-growing cancers and is often difficult to treat effectively using conventional methods such as surgery, radiotherapy, and chemotherapy. These treatments commonly damage healthy tissues, show poor drug penetration, cause severe systemic side effects, and frequently fail to deliver drugs deep enough to destroy all cancer cells leading to recurrence. Nanotechnology provides a superior and advanced approach by overcoming these limitations through targeted and controlled drug delivery. Nanoparticles such as liposomes, Ethosomes, solid lipid nanoparticles, metallic nanoparticles, polymeric nanoparticles, and nanofibers enhance drug stability, improve skin penetration, increase bioavailability, and deliver anticancer agents precisely to tumour cells while minimizing harm to normal tissues. Studies reviewed in this project clearly show that nanoparticle-based therapies achieve higher therapeutic efficiency, better tumour targeting, and fewer side effects compared to traditional treatments. Therefore, nanotechnology offers a more effective, selective, and safer strategy for the diagnosis and treatment of skin cancer.

KEYWORDS: Nanotechnology, nanoparticles, skin cancer, targeted drug delivery, SLNs, liposomes, metallic nanoparticles, nanofibers, polymeric nanoparticles.

2. INTRODUCTION

Skin cancer remains one of the most challenging diseases to manage because conventional treatments often lack precision, damage healthy tissues, and can lead to significant side effects. Traditional approaches such as surgery, chemotherapy, radiotherapy, and topical therapies mainly target cancer cells at the tissue level. In contrast, cancer itself originates at the cellular and molecular level. This gap between the target site and treatment depth often limits the effectiveness of standard therapies.

Nanotechnology bridges this gap by introducing materials at the nanoscale (1–100 nm)—the same scale as DNA, proteins, and cellular structures. Because nanoparticles can directly interact with cancer cells at a molecular level, they provide a highly focused, efficient, and safer method to detect, target, and eliminate skin cancer cells. Their unique physicochemical properties—such as high surface area, tenable size, and customizable surface chemistry—make them significantly more advanced than conventional treatments.

Nanoparticles can be engineered to deliver drugs exactly where they are needed, release them in a controlled manner, avoid premature degradation, and minimize toxicity to healthy cells. This capability transforms the treatment approach from being generalized to highly precise. As a result, nanotechnology offers a powerful strategy to treat melanoma, basal cell carcinoma, and squamous cell carcinoma with greater accuracy and fewer side effects.[1-2]

2.1 Why Nanotech & Nanoparticles Are Better for Treating Skin Cancer

1. Enhanced Targeting of Cancer Cells

Nanoparticles can be designed to recognize specific receptors overexpressed on skin cancer cells. This allows them to selectively accumulate in tumours' rather than spreading throughout the body. Reduces drug wastage, minimizes harm to healthy skin and surrounding tissues, increases treatment accuracy compared to chemotherapy or radiotherapy.

2. Improved Drug Delivery Efficiency

Most conventional drugs degrade before reaching the tumour or fail to penetrate deeply into cancerous tissue. Nanoparticles protect the drug from early breakdown and ensure it arrives efficiently at the cancer site.

Superior because ensures higher concentration of drug inside the tumour & it Works even on deeper or resistant cancer cells reduces required drug dose.

3. Controlled and Sustained Release

Nanoparticles allow slow, continuous release of anticancer drugs inside the tumour.

Advantages over traditional creams or injections maintains therapeutic levels for longer

Prevents sudden spikes in drug toxicity Reduces frequency of treatment

4. Ability to Bypass Biological Barriers

The skin is a strong protective barrier. Many drugs cannot penetrate it effectively. Nanoparticles, due to their small size, can easily cross the stratum corneum, enter deeper layers, and reach tumour cells.

5. Reduced Side Effects

Traditional cancer treatments cause inflammation, redness, blistering, and systemic toxicity.

Nanoparticles minimize these by delivering drugs only to cancer cells.

Why better: Less damage to healthy skin, better cosmetic outcomes, Lower risk of long-term complications.

6. Multi-Functional Treatment Capability

Nanoparticles can combine multiple actions in one platform—for example:

drug delivery imaging or diagnosis photothermal therapy This creates a “theragnostic” system—therapy + diagnostic tool in one.

Why better

Enables real-time monitoring of treatment

Improves treatment planning

Reduces need for multiple procedures Advantages of Nanotechnology in Skin Cancer Treatment.[3]

2.2 Advantages

1. High Precision and Selectivity
2. Increased Drug Solubility and Stability
3. Deep Penetration into Tumour Tissue
4. Ability to Deliver Multiple Drugs
5. Reduced Systemic Toxicity

6. Compatibility With Modern Therapies

7. Faster Healing and Better Cosmetic Results.[4]

2.3 Types of nano particles

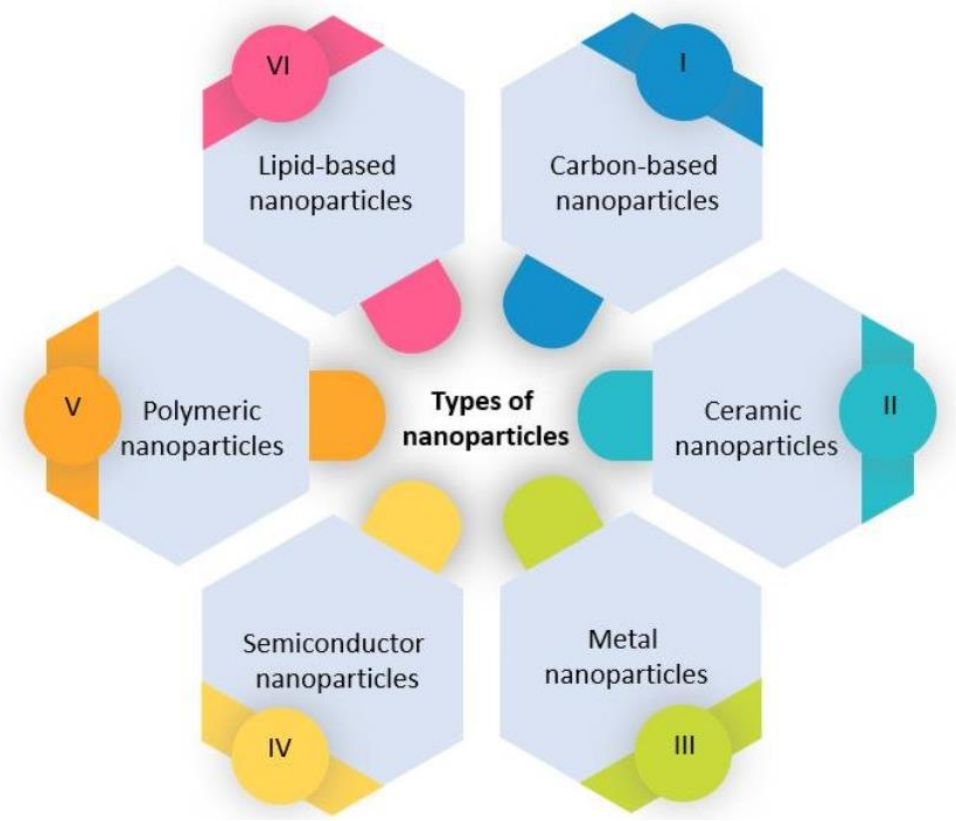

Figure 1: Schematic diagram representing the various types of nanoparticles.

3. LITERATURE REVIEW

1-Singh et al.; (2009) reported that nanoparticle-based drug delivery significantly increases therapeutic precision by directing drugs specifically toward tumor tissues. Their work explained how nanoparticles improve bioavailability and allow controlled release of chemotherapeutic agents. The study also noted reduced toxicity to surrounding healthy cells. These findings support the advantage of nanocarriers compared to traditional systemic treatments. This aligns with the project's aim to improve skin cancer therapy using targeted nanotechnology.

2-Chung et al.; (2020) explored nanoparticle applications in both cancer imaging and therapy, highlighting their dual diagnostic and therapeutic roles. Their research showed that nanoparticles enhance contrast in imaging, making early skin cancer detection more effective. They also discussed how nanocarriers improve drug solubility and targeting. The study

emphasized that nanotechnology provides multi-functional platforms for treatment. This supports the project's focus on advanced nanotechnology for managing skin cancer.

3-Youssef et al.; (2022) reviewed a variety of nanotechnology-based treatment strategies specifically for skin cancer, including lipid nanoparticles, polymeric carriers, and metallic nanostructures. The authors found improved penetration through skin layers and better localization of drugs at cancer sites. Their work also highlighted lower systemic toxicity and improved therapeutic response. They concluded that nanoparticles offer advantages over conventional therapies. This directly strengthens the foundation of the project.

4-Golestani et al.; (2024) investigated lipid-based nanoparticles and demonstrated their enhanced dermal penetration in skin cancer therapy. Their study found that these nanoparticles improve drug retention within tumor tissues, leading to more effective treatment outcomes. The authors also emphasized improved stability and biocompatibility. They highlighted that lipid carriers outperform regular creams and gels used in dermatology. These insights support the project's emphasis on nanocarrier superiority.

5-Bhattacharya et al.; (2023) studied dacarbazine-loaded solid lipid nanoparticles designed to improve melanoma treatment. Their findings showed significantly greater drug accumulation in melanoma cells compared to free dacarbazine. The study also demonstrated reduced inflammation and enhanced therapeutic retention. They concluded that SLNs improve both drug stability and tumor response. This directly supports nanoparticle-based chemotherapy as highlighted in the project.

6-Wang et al.; (2023) explored nanofiber-based targeted delivery systems that show strong potential for melanoma therapy. Their study demonstrated selective cytotoxicity toward cancer cells with minimal damage to surrounding tissue. They also reported sustained drug release from nanofibers, improving long-term treatment effectiveness. The authors explained that nanofibers can be engineered to guide drugs directly into tumour regions. This supports the project's focus on targeted nanotechnology formulations.

4. NEED OF STUDY

Skin cancer has become one of the most common and rapidly increasing cancers worldwide. Factors such as excessive exposure to sunlight, depletion of the ozone layer, environmental changes, and lifestyle habits have contributed to the rise in skin cancer cases. Although

treatments like surgery, radiotherapy, and chemotherapy are commonly used, they often have several disadvantages. These treatments can damage healthy tissues, cause severe side effects, and may not completely remove or destroy cancer cells, leading to recurrence of the disease. Many anticancer drugs also face problems such as poor penetration into the skin, low effectiveness, and rapid elimination from the body, which reduces their therapeutic impact.

Because of these limitations, there is a strong need for new and improved treatment approaches that are safer, more effective, and capable of targeting cancer cells specifically without harming normal tissues. Nanotechnology offers a promising solution to overcome these challenges. Nanoparticles can deliver drugs directly to cancer cells, improve drug stability, increase absorption through the skin, and provide controlled release of medication. This reduces side effects and improves treatment outcomes. Therefore, studying nanotechnology-based treatment methods is important to develop better therapies for skin cancer that can enhance patient recovery, reduce complications, and improve overall quality of life.

5. SKIN CANCER STATISTICS

5.1 Skin Cancers

Skin cancers most often are divided into two groups: non-melanoma (NMSC) and melanoma (*malignant melanoma*; MM)

The NMSCs can be distinguished into basal cell carcinoma (*carcinoma basocellular*; BCC) and squamous cell carcinoma (ratio of incidence compare with SCC is between 10:1 and 1:1) . MM accounts for 1.5–2% of all skin cancers Basal cell carcinoma is characterized by slow growth and slight and locally located malignancy. The development of BCC is favoured by precancerous conditions or previously unchanged skin and exposure to UV radiation (280–320 nm), but BCC can also affect the fatty tissue under the skin or spread even more. The highest rate of morbidity is observed in people over 65 years of age, which is more than 95% of all basal cell carcinomas Potential tumour-promoting factors include solar radiation (UVB), long-term exposure to exposed body parts, arsenic-type chemicals, soot, HPV viruses, and X-rays.[9-10]

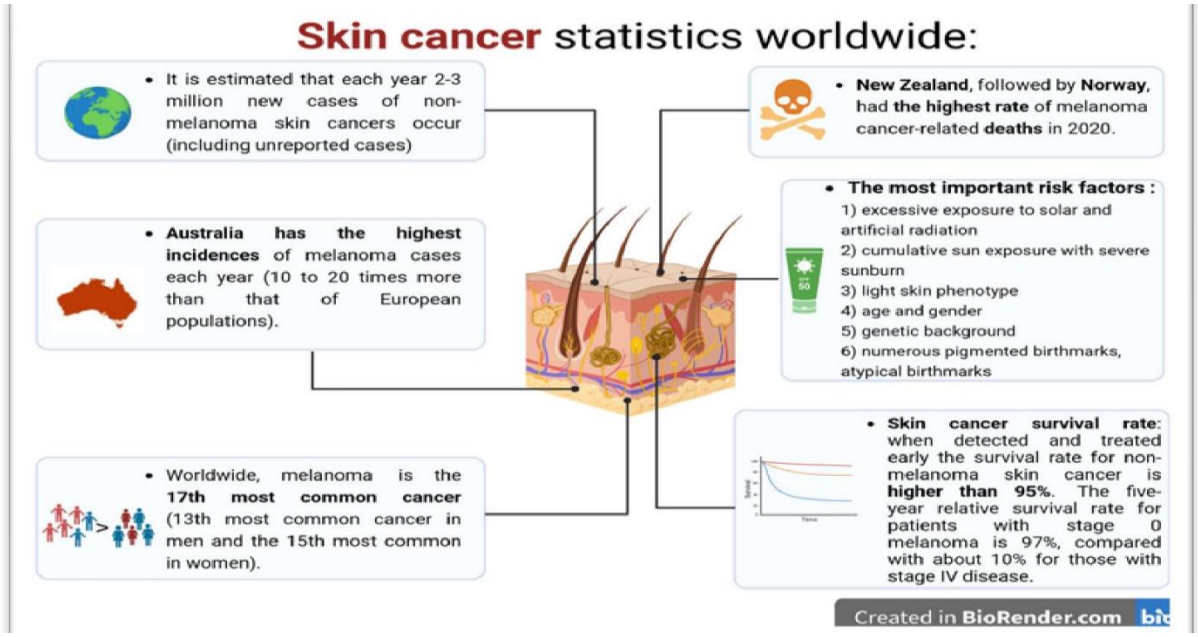

Figure 2. Skin cancer statistic based on WCRFI, WHO and American Cancer Society.

Precancerous conditions include actinic/actinic keratosis (keratosis senilis / actinic) with a risk of transformation, Xeroderma pigmentosum as a genetic defect (increasing the incidence of skin neoplasms), radiation dermatitis (radiodermatitis), as well as chronic inflammation, scarring or hypertrophic burn scars.

Squamous cell carcinoma develops from flat squamous cells that form a significant proportion of the epidermis (keratinocytes), the outermost layer of the skin.

Squamous cell carcinoma develops from flat squamous cells that form a significant proportion of the epidermis (keratinocytes), the outermost layer of the skin.

Squamous cell carcinomas usually grow slowly and often spread or metastasize. Basal cell carcinoma can also affect the fatty tissue under the skin or spread even more.

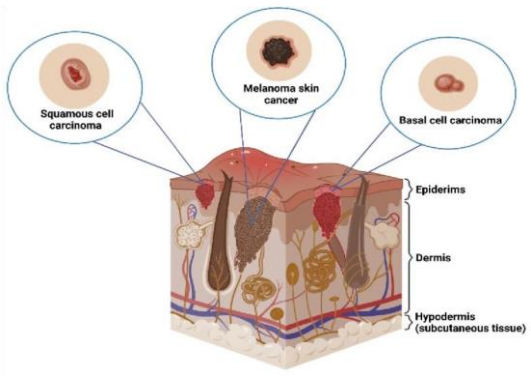

Figure3. Types of skin cancers.

Melanoma is one of the most aggressive cutaneous malignancies and it was first described in 1812 by Rene Laennac.

The tumour originates from the malignant transformation of pigment cells, i.e., melanocytes responsible for melanin synthesis.

Usually, melanoma is formed de novo but can develop based on damaged skin or skin lesions (pigmented nevi). The incidence of melanoma has increased dramatically in recent years. Over the past fifty years, there has been a five-fold increase in the incidence of melanoma among pale-skinned people.[11-12]

5.2 Nanotechnology in treatment of skin cancer

The fight against cancer must be supported to improve overall health in both Europe and elsewhere. Most current research aims at the early detection and effective treatment of oncological diseases, although some efforts are also made to improve the quality of life of patients, e.g., by pharmacoloically reducing pain, which is often an inherent element of the disease. Despite the enormous progress of modern medicine and the dynamic development of pharmacology and intensive scientific research, no fully effective, minimally invasive anticancer chemotherapy currently exists. The clinician must choose from a range of cytostatic drugs, each with a unique mechanism of action and application in the treatment of specific types of tumours, e.g., alkylating cytostatic drugs that disrupt the DNA structure of cancer cells (e.g., cyclophosphamide, cisplatin), antimetabolites that affect nucleic acid synthesis (5-fluorouracil [5-FU], methotrexate), microtubule-targeting drugs that prevent normal cell division (paclitaxel), and anthracycline antibiotics that disrupt DNA function (doxorubicin). Unfortunately, due to their non-specific activity towards cancer cells, many anticancer therapies have undesirable side effects and must be administered at high doses which are toxic to healthy tissues. Moreover, these drugs are often used in various combinations, depending on the type of tumour and its response to treatment. The most serious complications of chemotherapy are cardiotoxicity, hepatotoxicity, neurotoxicity, and nephrotoxicity, which may appear even many years after the end of therapy. Therefore, a great challenge for modern oncology is the development and synthesis of effective yet safe anticancer drugs with very low, or no, systemic cytotoxicity against normal cells, no side effects during and after the therapy, high specificity of action against cancer cells, and rapid elimination from the body in the least burdening way, and which are characterized by a lack of immunogenicity and mutagenicity.[13]

Great hopes are currently associated with nanotechnology, a new interdisciplinary branch of science and technology dealing with the design and creation of structures called nanoparticles, which range in size from 5 to 100 nm. It is currently one of the most popular fields of science and its development is of great importance in pharmacy and medicine. In recent years, nanotechnology has been of particular interest due to the high anticancer potential, relatively high durability, and low cytotoxicity of nanoparticles to normal cells. Recent development in nanotechnology provides the opportunity to effectively treat cancer by increasing the bioavailability, targeting, and delivery of drugs at effective concentrations to cancer cells; such developments also avoid the phenomenon of drug resistance.[14]

Current methods of treating skin cancers include photodynamic therapy, radiotherapy, and surgical excision of the tumour with a margin of healthy tissue. Conventional chemotherapy plays a limited role in treatment, especially in the case of melanoma. Occasionally, it is used after the surgical removal of the tumour to eliminate any potential cancer cell remnants, and in advanced stages of melanoma when the cancer has spread to other organs. Unfortunately, the effectiveness of chemotherapy in melanoma is limited, leading to the inclusion of alternative treatment methods such as immunotherapy and molecular and targeted therapies. Chemotherapy is used slightly more often in the treatment of other types of skin cancers, such as basal cell carcinoma or squamous cell carcinoma, especially in advanced cases.[15]

A growing number of in vitro and in vivo studies suggest that nanotechnology may be effective in the treatment of skin cancer. Nanomaterials and nanocarriers allow the development of drug delivery systems with greater biological effectiveness at lower doses and lower side effects. Due to the small size and surface characteristics of nanomaterials, the anticancer drugs loaded into such nanoparticles easily penetrate cell membranes and can be delivered directly and specifically to skin cancer cells, where they can then exhibit maximum effect. In addition, due to the increased activity of anticancer drugs administered by nanocarriers, the systemic side effects of chemotherapy are reduced; anticancer drugs that demonstrate greater effectiveness at lower doses play a key role in improving the overall health of patients. It should also be emphasized that the use of appropriate nanocarriers can counteract the biodegradation of cancer drugs in the patient’s body, reduce their removal from cells, or extend their half-life.[16]

Various nanostructured platforms, including liposomes, carbon nanotubes, nano micelles, nano emulsions, and metal nanoparticles have been explored for their potential in enhancing skin cancer diagnosis and treatment. These nano systems offer unique advantages in targeting tumour cells, enhancing drug delivery, and improving therapeutic efficacy.[17]

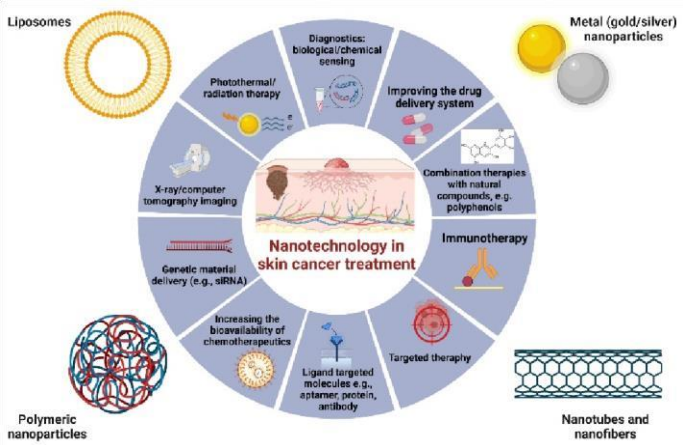

Figure 4. Strategies for the use of nanotechnology in the diagnosis and treatment of skin cancer.

5.3 Method used in treatment of cancer

1- Lipid based nanoparticles in skin cancer

2-Inorganic nanoparticles

3-polymer based nanoparticles.

- **Drug/nanoparticles used in the treatment of skin cancer**

1-Liposomes

2-Ethosomes

3-Nanofibres

4-Polymeric nanoparticles

5-Dendrimes

5.3.1 Lipid based nanoparticles in skin cancer

Lipid formulations have emerged as a promising technology to enhance drug efficacy and safety. By selectively delivering drugs to specific cells and organelles, lipid formulations can reduce side effects and improve treatment outcomes. Additionally, lipid formulations can stabilize drugs, making them easier to store and transport Among the various lipid formulations, lipid nanoparticles are particularly promising due to their unique composition

and structure. These spherical vesicles can solubilize and deliver drugs efficiently, improving their bioavailability and therapeutic potential.

Lipid-based nanoparticles are considered to be one of the most suitable carrier systems for therapeutic compounds due to their unique lipid composition Lipid nanoparticles are a diverse group, including liposomes, ethosomes, noisome and solid lipid nanoparticles Each with its unique properties and applications. Despite this, extensive research has been conducted on these compounds to evaluate their effectiveness in delivering anticancer therapies for various cancers, including skin cancer, while minimizing side effects.[18]

- **Liposomes**

Liposomes have become a universal tool in biology, biochemistry and pharmacy due to their great structural diversity. They are made of a lipid bilayer surrounding a central aqueous space containing the transported drug or other bioactive molecule. The use of liposomes enhances the biological effectiveness of routinely administered chemotherapeutic agents at significantly lower concentrations. This provides hope for patients in reducing the unfavourable side effects commonly observed during chemotherapy. This can be attributed to improvements in pharmacokinetic parameters, such as better drug/biomolecule delivery to cancer cells and overcoming both hydrophobic and hydrophilic barriers.

The fact that liposomes are rapidly taken up by the reticuloendothelial system and degraded by macrophages is an undeniable limitation. Negative aspects associated with their use as drug carriers can be eliminated by modifying their surface, for example, by introducing PEG polymers or cationic lipids into their structure. These chemical modifications effectively enhance the pharmacokinetic and pharmacodynamic properties of the liposomes. It is important to note that one of the most commonly used methods today is to coat the surface of the liposome with polyethylene glycol (PEG), creating what is known as long-circulating liposomes or ‘stealth liposomes. Obviously, it is possible to further modify the surface of the liposomes by incorporating various ligands onto the surface of the liposome, such as glycoproteins, immunoglobulins, peptides, transferrin, etc., in order to preferentially target them to overexpressed receptors in tumour cells.[19]

Many strategies have been trailed for utilizing liposomes in the treatment of skin cancer. These involve both the use of routinely administered chemotherapeutic agents (e.g., doxorubicin or fluorouracil) natural polyphenols as chemotherapy adjuvants (resveratrol,

curcumin, epigallocatechin) and gene therapies, such as the application of siRNAs to modulate the expression of specific genes of cancer cells Encapsulation of doxorubicin, paclitaxel, or 5-fluorouracil improves their pharmacokinetics, thus increasing their half-life in cancer cells. Sing et al. showed that the encapsulation of DOX and celecoxib (CEL), a non-steroidal anti-inflammatory drug, in liposomes significantly increased the biological activity of chemotherapeutic agents in human skin carcinoma A431 cell culture. These dual drug-loaded liposomes were able to inhibit cancer cell viability by up to >99%, even at lower concentrations. The co-exposure of doxorubicin and celecoxib synergistically inhibited the AKT and COX-2 pathways leading to cell apoptosis.[20]

The progression and metastasis of skin cancers is often associated with the overexpression of receptors for growth factors, such as the epidermal growth factor receptor EGFR on the surface of tumour cells. Some of the most promising nanocarriers for targeted drug delivery in skin cancer treatment are receptor-specific liposomes, conjugated with appropriate ligands. This technique has been combined with the use of aptamers due to their ability to recognize antigens, ease of chemical variability, and sequence changes. One study examined the drug release kinetics, in vitro cell viability, in vitro targeting capability, and apoptotic effects of a combination of AS1411 aptamer-functionalized liposomes loaded with 5-FU on human dermal fibroblasts (HDF) and the BCC cell line TE 354.T

It has been shown that aptamer conjugation increased liposome size and reduced the surface potential of the liposomes; moreover, the aptamer moieties increased the stability of the liposomes and acted as a supplementary steric barrier leading to a lower cumulative amount of the released 5-FU. The results indicate that aptamer conjugation increased liposome size and reduced the surface potential of the liposomes, and that the aptamer moieties increased the stability of the liposomes and acted as a supplementary steric barrier, reducing the cumulative amount of the released 5-FU. The results indicate that the functionalized liposomes are more efficient as nanocarriers than the non-functionalized ones. The therapeutic effect of 5-FU was also improved by eliminating a number of secondary, undesirable effects which accompany the classic one-drug administration.[21]

AS1411 aptamer-functionalized liposomes loaded with 5-FU may have potential as effective and targeted treatment in basal cell carcinoma (BCC). The use of the AS1411 aptamer is significant because it specifically binds to nucleoli, a protein present in the cell membrane of various cancer cells, including basal cell carcinoma (BCC). Petrilli et al. Evaluated the

potential of EGFR targeted immuno-liposomes, composed of cetuximab encapsulated by 5-FU, against squamous cell carcinoma (SCC) in vitro using A431 (EGFR positive) and B16F10 (EGFR negative) cell lines, as well as in an in vivo animal model.

Currently, great expectations in cancer treatment are associated with gene therapy and the use of miRNA, siRNA, and shRNA. Appropriate modulation of genes associated with the proliferation of cancer cells can inhibit cancer progression, block the cell cycle and ultimately cause cell death, e.g., by apoptosis. Numerous studies indicate that the use of siRNA particles encapsulated with liposomes yields very good results in the treatment of skin cancer. The main targets for this therapy comprise the genes/pathways responsible for the proliferation of cancer cells. Interesting results were obtained for siRNAs inhibiting the Akt and MAPK/PI3K pathways and c-my gene activity; the suppression of c-My production in tumours inhibited tumour progression in mouse models.[22]

- **Ethosomes**

When discussing lipid nanoparticles, it is important to mention the increasing popularity of ethosomes. Ethosomes are an area of rapidly growing research, with studies investigating their potential to treat a wide range of diseases. This nanocarrier system shows promise for various medical applications. Ethosomes, which contain ethanol in their formulation, have unique properties that distinguish them from liposomes. Due to the presence of alcohol, It has been found that there are a number of unique properties that can improve the efficacy and safety of drug delivery. Ethosomes are a promising but relatively unexplored delivery system that holds immense potential for improving melanoma treatment. Recent studies have demonstrated their ability to effectively penetrate the skin and selectively deliver drugs to melanoma cells, leading to enhanced therapeutic outcomes. However, more extensive clinical trials are needed to firmly establish the safety and efficacy of ethosomes as a melanoma treatment modality.

Several recent studies, both in vitro and in vivo, have demonstrated that combining ethosomes with classical chemotherapy and drugs can be an effective treatment. Khan and Wong's study showed that encapsulating 5-FU into ethosomes significantly increased drug penetration into the skin and retention, resulting in increased effectiveness of the chemotherapy drug. In relation to this study, there are also results from another team of researchers who have used a combination of mitoxantrone and ethosomes. They observed a

higher permeability of nanoparticles through the skin of rats and a significantly higher in vivo antimelanoma effect than MTO solutions.

It is important to note that the enhanced efficacy of drugs when combined with ethosomes is not limited to traditional chemotherapeutic agents like 5-FU or paclitaxel. In recent research, Mousa et al. achieved compelling in vitro and in vivo results with encapsulated metformin. The compound inhibits the growth of skin cancers in vitro. However, the use of appropriate ethosomes significantly increased the antitumor activity against skin cancer compared to the application of free metformin in male Swiss albino mice. It is important to note that satisfactory results have been obtained in studies using a combination of ethosomes and natural compounds that not only have cytotoxic properties, but also contribute to redox homeostasis and inhibit the generation of free radicals in skin cancer cells.

Studies conducted by independent research teams using compounds such as epigallocatechin, nobiletin or fisetin indicate that the combination of natural compounds with ethosomes increased their activity in skin cancer cells compared to non-encapsulated solutions of phytochemicals. The authors emphasize that better anticancer effectiveness results from the increased availability of phytochemicals and their better accumulation directly in the environment of skin cancer cells. Histopathological analyses conducted in in vivo studies showed a reduction in tumour size in mice after the administration of nanoparticles. Furthermore, biochemical quantification of oxidative stress biomarkers, such as glutathione, superoxide dismutase, and catalase, indicated better inhibition of reactive oxygen species generation in skin cancer cells treated with phytochemicals encapsulated in ethosomes.[23]

- **Solid Lipid Nanoparticles**

Solid lipid nanoparticles (SNLs) are colloidal lipid carriers with a typical size range of 50–1000 nm. The SLNs are composed of natural lipids, including fatty acids, steroids, waxes, monoglycerides, diglycerides, and triglycerides. The solid lipid core matrix fowls encapsulates lipophilic or hydrophilic drugs, depending on the preparation method. Surfactants are used to stabilize the core lipid matrix. However, their ability to encapsulate anticancer agents and safely transport them to the tumor site for controlled release, without causing any permeability or toxicity issues, has made them the most competitive drug carriers for skin cancer therapy.

According to Kim et al.'s research, the encapsulation of docetaxel into SNLs led to a significant improvement in the drug's biological activity against melanoma. It inhibited growth and prevented tumour formation in mice, which was significantly superior to the administration of free docetaxel. Additionally, the treatment resulted in an increase in the population of cytotoxic T cells, while the population of tumour-associated macrophages and regulatory T cells decreased.

In line with these reports are also recent studies using 5-FU and dacarbazine [The use of SNLs for drug encapsulation resulted in a significant improvement in their anticancer properties, increased drug retention and bioavailability. Histopathological analysis showed that rats treated with dacarbazine-SNLs had less keratosis, inflammatory responses, and angiogenesis than rats treated with free dacarbazine. Similar effects were observed in independent studies in in vitro and in vivo experiments. Mice treated with 5-FU-SNL exhibited decreased inflammatory responses, less keratinization, and reduced signs of angiogenesis when compared to mice treated with 5-FU.[24]

5.3.2-Inorganic nanoparticles

Inorganic nanoparticles have shown considerable potential in the fight against cancer. They can deliver drugs directly to cancer cells, image cancer lesions, and enhance the effects of radiotherapy. Nanoparticles can be produced from various materials, including metals and their oxides, carbon, or silica. Their unique properties, such as small size, large surface area, bioactivity, biocompatibility, and modifiability, make them ideal candidates for skin cancer therapy. Various strategies exist for utilizing inorganic nanoparticles in anticancer therapy. While some molecules possess antiproliferative properties, they are also used as effective drug carriers or as photosensitizers in classical photodynamic therapies.[25]

- **Functionalized Metal Nanoparticles**

Currently, gold and silver nanoparticles are most often used in the treatment and therapy of skin cancer and have been thoroughly tested in recent years. Due to their small size, these molecules easily penetrate healthy cells and accumulate in cancer cells, ensuring high concentrations of chemotherapeutic agents in cancerous cells. Gold and silver nanoparticles are used for administering targeted medication, monitoring tumour progress, vaccinations, and as potent chemical sensors or as elements of therapy combined with photodynamic therapy (PDT).

Gold nanoparticles are of particular interest due to their potential to increase the activity of anticancer chemotherapeutic agents while reducing the side effects of treatment by enabling lower doses. One of the main strategies in the use of metal nanoparticles is their combination with available chemotherapeutic agents. The latest research shows that the use of gold and silver nanocarriers in combination with 5-FU significantly increases its anticancer activity. Greater cytotoxicity of the drug was observed in relation to conventional chemotherapy. It was shown that metal nanocarriers increased drug stability and clearly improved its pharmacokinetics in cancer cells. The higher concentration of 5-FU in cancer cells and the targetability resulted from a much better penetration of cancer cells by nanoparticles than in the case of 5-FU used alone.

The results obtained were highly satisfactory. A significant decrease in tumour cell proliferation was observed compared to controls, and the nanoparticles demonstrated immunomodulatory properties: treatment was associated with a decrease in serum proinflammatory cytokines, including tumor necrosis factor TNF alpha and beta, nuclear factor kappa B (NF-kB), and interleukins 1 and 10 (IL-1, IL-10). This resulted in apoptosis, probably due to, inter alia, the generation of ROS in cancer cells and lipid peroxidation gold nanoparticles encapsulated with methotrexate also yielded good results against moderate to severe inflammatory diseases, as noted on in vivo and in vitro skin models. Topical treatment with AuNPs-3MPS@MTX reduced keratinocyte hyperproliferation, epidermal thickness, and inflammatory infiltration in vivo in a mouse model of imiquimod induced psoriasis.

A promising approach is to combine natural phytochemicals with metal nanoparticles of gold or silver. Combining polyphenols with nanoparticles has been found to yield synergistic anticancer properties. Numerous studies using curcumin indicate that nanoparticles significantly contribute to improving the antiproliferative properties of phytochemicals against skin cancer. As in the case of chemotherapeutics, such improvements have been attributed to enhanced distribution and release of polyphenols in cancer cells. Importantly, such combinations often induce apoptosis in skin cancer cells. The studies showed an increase in the activity of anti-apoptotic BH3-only proteins from the Bcl-2 family and a simultaneous decrease in their anti-apoptotic partners.[26]

It is believed that these pro-apoptotic properties are based on the pro-oxidative activity of the compounds and the generation of significant amounts of ROS in cancer cells. Modern therapies often use radiotherapy to increase the effectiveness of metal nanoparticles. PDT

(photodynamic therapy) has been found to be particularly effective, and is becoming increasingly popular for treating various types of cancer, including skin cancer, However, the organic photosensitizers used in PDT are often burdened with numerous disadvantages, such as high systemic toxicity, low selectivity of action towards cancer cells or low level of light absorption.

Noble metal nanoparticles are characterized by high chemical and physical stability, minimal toxicity to normal cells, and high selectivity of action, and are gaining popularity as photosensitizers. The latest research shows that gold and silver nanoparticles can be successfully used in modern photodynamic therapies. The molecules are characterized by good biocompatibility and bioavailability, with a clear accumulation in the tumour, which additionally significantly improves the effectiveness of photothermal therapy (PTT) or PDT in the treatment of melanoma. Xie et al. report that gold nanoparticles not only yielded a potent PTT/PDT effect on destroying the primary tumours, but also elicited strong antitumor immunity for eliminating primary and metastatic melanoma; they can also relieve immune suppression by promoting T cell infiltration into tumours, and maintain lasting anti-tumour immunity for long-term prevention of melanoma recurrence.

Metal nanoparticles have also been used to support biopsy and radiotherapy, which may not be sensitive enough to detect melanoma at an early stage. Surface-enhanced Raman spectroscopy (SERS) is gaining popularity in bioimaging and diagnostics. Au NPs (nanoparticles) are considered excellent for in vivo imaging applications because they are inert, biocompatible, and their localized surface plasmon resonances (LSPR) can be aligned towards near infrared (NIR) regions.[27]

- **Carbon Nanotubes**

Carbon nanotubes are characterized by a unique structure with interesting optical, chemical, physical, and mechanical properties. One of the advantages of nanotubes is their ability to penetrate cell membranes and carry small molecules or biological macromolecules such as plasmids, siRNA, or proteins into cells. They can be used as a biomarker sensor for the diagnosis of skin melanoma and infection at an early stage. Moreover, carbon nanotubes offer targeted delivery to the cancerous cells, act selectively, and provide better penetration in the neoplastic cells due to improved permeability and retention effect. Several studies indicate that the use of carbon nanotubes improves the effect of drugs and affects the chemical stabilization of chemotherapeutic agents. Sahoo et al. found carbon nanotubes combined

with graphene oxide loaded with the anticancer drug calprotectin to effectively inhibit the proliferation of breast and skin cancer cells.[28]

- **Nanofibers**

The use of nanofibers in treatment can be very diverse, and as research shows, they can be a good transporter for both natural compounds and synthetic chemotherapeutics. Rengifo et al. report that the use of appropriate nanofibers in combination with an anticancer compound may not only increase its cytotoxicity. Studies on B16F10 melanoma cells showed that nanoparticle delivery significantly improved control of drug release in local chemotherapy of skin cancer. Nanoencapsulation increased both skin compound permeation and retention. A recent study by Bala Shanmugam et al. found polymers composed of photosynthesized AuNPs and curcumin for the treatment of skin cancer A431 cell to exhibit selective toxicity; nanofiber treatment induced apoptotic death in cancer cells but not in normal cells.

Nanofibers are also successfully used in combination with commercially used drugs, e.g., metformin, or commonly used chemotherapeutics, such as 5-FU, etoposide, and methotrexate. the use of metformin surface modified cellulose nanofiber gel resulted in a significant decrease in the invasiveness of murine melanoma cell B16F10. Treatment yielded high suppression of skin cancer cell migration and a significant inhibition of their proliferation and growth. This indicates that the strategy is a promising approach for preventing melanoma metastases

Extremely valuable results were achieved regarding the use of cellulose nanofibers modified with Fe_3O_4-Ag_2O quantum dots as a carrier of anticancer drugs for skin cancer. Importantly, while these compounds exhibited very low cytotoxicity against normal cells, they also demonstrated considerable potential against skin cancer cells. The drug was found to have greater anticancer potential and cytotoxicity against the human melanoma SK-MEL-3 cell line, which may have been due to its selective release.

Zhu et al. report that the use of appropriate, novel core-shell nanofibers based on chitosan (CS)-loaded poly (ε-caprolactone) and a 5-fluorouracil (5-FU)-loaded Poly(N-vinyl-2pyrrolidone) (PVP) core increased the anticancer activity of the chemotherapeutic agent against melanoma skin cancer cells (B16F10 cells). The nanoparticle showed significant inhibitory proliferation effects on B16F10 cells in vitro through arresting cell cycle progression at S phase and G2/M phase in time-dependent manner. More importantly, 5-FU

in this form showed significantly less activity against normal cells. This data hints at a promising future cancer treatment strategy, and the potential for synergism may expand the possibilities of designing chemotherapy therapy with minimal adverse effects on normal cells.[29]

5.3.3 polymer-based nanoparticles

Polymer-based nanoparticles are drug carriers made from synthetic or natural polymers. They are divided into different types based on their shape and the properties of the polymer used, such as micelles, dendrimers, polymer Somes, and polyplexes. These nanoparticles have several advantages, including improved preparation techniques, biocompatibility, biodegradability, and lower production costs. From a biological perspective, polymer-based molecules possess several advantageous characteristics. These nanoparticles can conjugate, adsorb, capture, or encapsulate anticancer agents, including hydrophilic and lipophilic drugs, monoclonal antibodies, and genes, among others, for controlled release, tumour targeting (active/passive), protection under physiological conditions, and enhanced tumour uptake.[30]

- **Functionalized Polymeric Nanoparticles**

Polymer nanoparticles can increase the efficiency of transport of used drugs and proteins to target cells to reduce their toxic effects. Their nanoscale size allows them to effectively penetrate cell membranes and increase their stability, which allows the drug to stay in circulation longer. The anticancer effects of most melanoma anticancer drugs are limited due to their lipophilic structure and hence unfavourable pharmacokinetic and pharmacodynamic properties. However, the free drug release profile of anticancer drug formulations has been improved by the use of amphiphilic polymers, i.e., those with both hydrophobic and hydrophilic sections.[31]

Polymer nanoparticles offer promise due to their greater stability, controlled release, and enhanced skin permeation. Different forms of polymer nanoparticles, such as nanospheres and nano capsules, polymer micelles, dendrimer-based micelles, and polymer drug conjugates, can be produced by altering the properties of the polymer. Zou et al. [report that, like liposome systems, polymer nano systems can not only significantly improve CT scan imaging of tumours, but also mediate effective targeted chemotherapy for melanoma. Natural polymeric nanoparticles like chitosan, gelatine, albumin, and alginate are most frequently used for topical skin delivery and targeting skin melanoma. These compounds are often

characterized by high chemical stability and good penetration of skin cells and possess very valuable antioxidant, antibacterial, and anti-inflammatory properties.[32]

There are many strategies for using polymer nanoparticles in the diagnosis and effective treatment of skin cancer, depending on the carrier molecule and the type of active substance being transported. It is possible to transport siRNA to inhibit the expression of key genes for melanoma cell proliferation. Very promising results were obtained by Scopel et al. who synthesized hybrid lipid-polymer nanoparticles with high affinity for the vitamin D3 receptor on the surface of B16 melanoma cells. Cell uptake experiments found the nanoparticles to effectively target B16 melanoma cells, thus offering a promising vehicle for delivering therapeutic agents for the treatment of melanoma. This method is therefore an excellent starting point for the development of targeted melanoma treatment protocols and the specific delivery of encapsulated therapeutic agents to other cells containing nuclear vitamin D receptors.[33]

The use of a PDT photosensitive agent in combination with polymer nanocarriers was also proposed by Gamal-Eldeen et al., who encapsulated indocyanine green (ICG) in polymer nanoparticles. Skin squamous cell carcinoma was induced in CD1 mice. The results clearly indicate that the ICG polymeric nanoparticles had high anticancer potential, with treatment resulting in decreased activity of TNF-L, COX-2 cyclooxygenase, and 5-LOX 5-lipoxygenase, which are involved in angiogenesis; treatment also resulted in enhanced apoptosis, caspase production, and histone acetylation.[34]

Xia et al. provided extremely valuable data on the use of the oncolytic peptide LTX-315 with polymeric nanocarriers in skin cancers. The results indicate that chimeric (carts as a robust systemic delivery vehicle for LTX-315 that enhances the immunotherapy of B16F10 malignant melanoma in mice when combined with a CpG adjuvant and anti-PD-1. A significant decrease in the proliferation of cancer cells was observed, as well as a strong immune response, which was confirmed by increased secretion of, inter alia, IL-6, IFN-γ, and TNF-α. The obtained results can undoubtedly open a new way to the development of oncolytic peptides, which enables permanent cancer immunotherapy through systemic administration.[35]

➢ **Dendrimers**

When discussing polymeric nanocarriers in the context of their use in the treatment of skin cancer, dendrimers cannot be omitted. The latest research undoubtedly reveals the very high attractiveness of these molecules and the possibility of their wide application in the diagnosis and treatment of skin cancer. In their study, Ybarra et al.

Proposed the use of dendrimers as nanocarriers for Vasogenic (VDG), an anticancer, first-in-class inhibitor of the Hedgehog signalling pathway, indicated for the treatment of locally advanced or metastatic basal cell carcinoma. The authors point to the development of interesting nano systems with potential utility in local treatment of basal cell carcinoma. Xia et al.[36]

Used a combined strategy of chemotherapy and immunotherapy against murine B16F10 melanoma cells by encapsulating doxorubicin in the G4 PAMAM dendrimer with additionally integrated molecule cytosine– phosphate–guanine-based oligonucleotides followed by heparin coating. The compound showed improved treatment efficacy in primary melanoma tumour and lung metastases. Immune activation and multiple antimetastatic effects of nanoparticles establishes a new therapeutic strategy for melanoma.[37]

5.4 Future Prospects of Nanotechnology in Cancer Therapy

Nanotechnology holds tremendous potential to revolutionize the future of cancer therapy through its ability to design highly precise, effective, and personalized treatment approaches. The current limitations of conventional cancer treatments—such as poor drug selectivity, systemic toxicity, and multidrug resistance—can be addressed through advanced nanocarrier systems. Future nanomedicine research is focusing on developing smart nanoparticles that can respond to specific stimuli within the tumour microenvironment, such as pH changes, enzyme activity, or temperature variations. These “stimuli-responsive” nanoparticles can enable on-demand drug release, ensuring that the therapeutic agent is activated only at the tumour site, thereby minimizing damage to healthy tissues.

Another promising area is personalized nanomedicine, where nanocarriers will be tailored according to individual patient profiles, tumour genetics, and biological markers. This personalized approach will improve therapeutic efficiency and significantly reduce unwanted side effects. In addition, multifunctional or theragnostic nanoparticles are being developed that combine therapeutic and diagnostic capabilities within a single platform. These systems

can deliver anticancer drugs while simultaneously allowing imaging and real-time monitoring of treatment response, making therapy more precise and adaptive.

Furthermore, nanotechnology-based immunotherapy is gaining momentum as nanoparticles can be used to modulate immune responses, deliver cancer vaccines, or enhance the activity of immune checkpoint inhibitors. The integration of nanotechnology with gene therapy and CRISPR-based genome editing tools also shows great potential for future cancer management, enabling targeted genetic correction of oncogenes or tumour-suppressor genes. Additionally, biodegradable and biocompatible nanomaterials are being explored to minimize long-term toxicity and environmental impact, ensuring safer clinical translation.

As nanotechnology continues to evolve, collaboration between materials scientists, oncologists, and pharmacologists will be essential to overcome challenges related to large-scale production, stability, and regulatory approval. With continued advancements.[39]

6. RESULT AND DISCUSSION

RESULT

The review of the collected literature showed that nanotechnology plays an important role in improving the treatment of skin cancer. Lipid-based nanoparticles, especially solid lipid nanoparticles, were found to enhance drug stability and allow controlled release, which increases drug concentration at the tumour site. Studies included in the project reported that solid lipid nanoparticles provide better drug retention in melanoma cells and show improved therapeutic effects compared to conventional drug delivery.

Metallic nanoparticles such as gold and silver demonstrated additional benefits by supporting photothermal and photodynamic therapy. These nanoparticles helped in increasing cancer cell death and improving treatment efficiency. Nanofiber-based delivery systems also showed promising results by providing sustained drug release and better skin penetration. Overall, the reviewed literature indicates that nanotechnology-based drug delivery systems offer more effective and targeted treatment options for skin cancer than traditional methods.

DISCUSSION

The findings from the reviewed literature suggest that nanotechnology has the potential to overcome many limitations of conventional skin cancer treatments. Traditional therapies often cause damage to healthy tissues and exhibit poor drug targeting. In contrast,

nanoparticles improve drug delivery by directing the drug specifically to cancer cells, reducing side effects and increasing treatment success. Solid lipid nanoparticles were identified as one of the most effective systems due to their ability to retain drugs in tumour tissue and provide controlled release.

Metal nanoparticles showed unique advantages by combining drug delivery with photothermal or photodynamic effects, making them suitable for combination therapy. Nanofibers further improved treatment by enhancing skin penetration and maintaining sustained drug levels. However, despite these positive outcomes, the reviewed studies also highlighted challenges such as safety concerns, large-scale production difficulties, and limited clinical approval. Therefore, while nanotechnology appears highly promising, further research and clinical evaluation are needed for its successful application in skin cancer treatment.

7. CONCLUSION

The conclusion of this review is by using specially designed nanocarriers—such as liposomes, metal nanoparticles, polymeric nanoparticles, nanofibers, and carbon nanotubes—therapeutic agents can be delivered directly to cancerous cells with greater precision and reduced toxicity. This targeted delivery not only enhances the effectiveness of treatment but also minimizes damage to healthy tissues, which is a major drawback of conventional therapies. The project also shows that nanoparticles support earlier detection of cancerous changes and enable more accurate monitoring of treatment response. Their improved selectivity, controlled drug release, and deeper tissue penetration explain why nanoparticle-based methods offer clearer advantages over standard treatments. Overall, the use of appropriate nanomaterials can increase therapeutic efficiency, lower required drug doses, and create a more patient-friendly approach for both diagnosing and treating skin cancer. Furthermore, the versatility of different nanoparticle systems allows treatment to be adapted according to tumour type, drug properties, and patient needs. This adaptability strengthens the potential of nanotechnology to achieve consistent therapeutic outcomes where traditional treatments often struggle. As demonstrated throughout the project, integrating nanotechnology into skin cancer management presents a promising pathway toward safer, more precise, and more effective therapeutic options for future clinical use.

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