Review Article

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Transdermal Drug Delivery in Oncology Charting the Road Ahead

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ABSTRACT

Transdermal drug administration is a method of administering medication through the skin that is non-intrusive, offering an innovative and hopeful alternative to traditional oral and injection methods. Advancements in skin penetration technology have enabled the transdermal administration of various anticancer medications, including lipophilic or hydrophilic compounds, offering a new approach to cancer treatment. Research has explored innovative platforms for cancer treatment, such as erythrocytes, vesicles, and exosomes. The most efficient approach is the transdermal drug delivery system. This review investigates various transdermal delivery techniques beyond the pharmaceutical sector in relation to cancer treatment. Techniques include iontophoresis, electroporation, sonophoresis, microneedles, transdermal patches, or vesicular systems like liposomes, niosomes, transferosomes, ethosomes, transethosomes, nanoparticles, carbon nanotubes, quantum dots, as well as nanofibers, which have been used to improve transdermal distribution and their use in cancer treatment. Additionally, a roadmap is presented to guide development strategies, highlighting the multiple applications of transdermal drug administration systems for cancer therapy.

Keywords: Transdermal drug delivery, Skin cancer, Breast cancer, Nanoparticles, Vesicular system

1. Introduction

One of the biggest threats to public health worldwide is cancer [1]. It has been estimated that contact with irradiation as well as chemicals that cause cancer accounts for 85–94% of cancer occurrences. According to information made public by the Skin Cancer Organization [2]. A kind of skin cancer appears in one out of three possible cancer cases. Exposure to the sun and sunburns are the primary factors that increase the likelihood of individuals developing melanoma. [3]. Research has suggested a reduction of the ozone layer leads to a higher intake of harmful UV radiation from the sun, resulting in an elevated risk of skin cancer [4]. Likewise, in both industrialized and emerging nations, breast cancer is the most prevalent form of cancer in women [5]. 285,220 new instances of aggressive breast cancer along with 43,120 new cases of non-invasive breast cancer were predicted to have been discovered in the United States within 2021 [6]. Aside from surgery, other cancer possibilities for therapy include traditional chemotherapy, radiation therapy, biological therapy, as well as immunotherapy. By boosting treatment efficacy and reducing adverse reactions, to both forms of immunotherapy or A few malignancies may be treated with transdermal medication delivery techniques, including lymphoma, skin, or distal organ carcinomas [7]. It is highly desirable to have compositions that are capable of permeating the dermis, providing prolonged release, or targeting tumors for better adherence from patients with improved therapeutic effectiveness, as well as decreased undesirable effects. The skin, as the biggest organ in the human anatomy, contains an outer coating that is almost impervious to outside elements such as substances, microorganisms, and particulates, including things that are colloidal. The skin's stratum corneum, the uppermost lipid-rich layer that covers the skin, can only be penetrated by medications with modest lipid solubility. While there are hydrophilic channels, secretions of sweat, and hair follicle pores, those compounds bearing moderate solubility in water or fats can pass through the skin or transdermal purposes [8]. The capability of a substance may pass through the skin is affected with its size, oil-water distribution, and charge on the surface [9]. Only molecules smaller than 35 nm may pass across its lipidic, as well as aqueous channels of the stratum corneum due to its porosity [10]. For a transdermal drug to be effective, it must be able to dissolve well in the lipid bilayers of the skin, as this is the step that controls the rate of drug absorption. Additionally, the drug needs to have sufficient permeability through the skin, be potent enough to reach therapeutic levels in the body, and not lead to any skin sensitivities or irritations.

1.1. Ideal properties for transdermal drug delivery

- The pH of the saturated aqueous solution needs to be between 5-9
- Drugs with a low melting point of less than 200°C should be used.
- Molecular weight should be less than 500 Daltons.
- It should have good spreadability and extrudability property
- It should be non-irritation and non-sensitization
- The lipophilic Nature Should be >1 and <4

1.2. The evolution of transdermal drug administration methods for cancer therapy.

During the 1960s, research efforts were directed towards examining the skin's capacity to block substances, with a particular emphasis on the stratum corneum, or skin layers. The groundbreaking research conducted by Scheuplein, Higuchi, and colleagues during the 1960s elucidated the mechanisms of passive percutaneous absorption [11]. During the 1990s, researchers started investigating utilizing liposomes in medical settings and progressed towards marketing them. From 1990 to 1994, numerous liposomal medications were introduced into clinical trials. An illustration of this is the liposome-encapsulated doxorubicin, which received considerable interest as a chemotherapy drug. In 1995, the Food and Drug Administration approved Doxil, the first liposomal medication [12]. In 2007, microneedles successfully pierced skin tissue without the need for penetration enhancers or specific insertion tools, as in previous research [13]. Electroporation therapy with cytotoxic drugs was termed electrochemotherapy in 2009. Bleomycin and cisplatin have shown encouraging promise in the therapy of some primary cancers, including head or neck squamous cell carcinomas along with basal cell carcinomas, as well as metastatic malignancies, such as melanoma [14]. In 2009, effective transportation of Novel Polyethylene

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glycol-coated niosomes utilizing bolasurfactant as a drug carrier for 5-fluorouracil, a commonly used anticancer agent for breast cancer treatment [15]. The 2010 study's goal was to create a transdermal patch with anastrozole embedded in the adhesive for targeted delivery to the breast tumor area, demonstrating the efficacy of this approach in reaching a high medication concentration at the location [16]. In 2010, research in this field has concentrated on creating various drug reservoirs that can transport high amounts of chemotherapy drugs to cancerous tissues while sparing cells and organs in the body's circulation. micelles used with ultrasound to target cancerous tissues [17]. A novel dendrimer nanocarrier with long circulation and pH sensitivity was developed in 2011 to deliver 5-fluorouracil to tumors by targeting nanoparticles to the acidic tumor environment [18]. In 2012, researchers created and analysed tamoxifen citrate-loaded ethosomes for use in transdermal treatments [19]. The formulation of Nanostructured lipid carrier (NLC) showed promise in 2013 as a carrier with cytotoxic effects and sustained release properties, allowing tryptanthrin to be absorbed by breast cancer cells [20]. In 2014, raloxifene hydrochloride-loaded nanotransferosomes were discovered to be an extremely effective treatment for postmenopausal women's osteoporosis and aggressive breast cancer [21]. The use of iontophoresis to improve the skin absorption of liposome-encapsulated curcuminoids (LEC) and assess the efficacy of mitoxantrone in dealing with breast carcinoma when its related lymph node metastases in conjunction with solid lipid nanoparticles (SLN) were studied in 2015 [22]. In 2016, a biocompatible or cell traceable system for drug distribution using Graphene Quantum Dots (GQD) was developed for the targeted transportation of the DNA intercalating drug doxorubicin (DOX) into cancerous cells [23]. In 2017, a new innovation was developed for treating skin and colon cancer: carbon nanotube and microsponge. [24]. In 2020 and 2021, biopolymeric polyvinyl alcohol/silver nanoparticles (PVA-AuNPs) and electrospun nanofibers loaded with PCL-Curcumin were developed, demonstrating possible anticancer effects against A431 skin cancer [25,26]. (Figure 1) represent historical evolution of transdermal method for administering drugs to treat cancer.

1.3. Various approaches of transdermal drug delivery systems

1.3.1. Electrically assisted methods

A. Iontophoresis

Iontophoresis, demonstrated to enhance skin absorption or elevate the release rate of several drugs that have low absorption/permeation rates, facilitates the movement of ions through the membrane when a minor externally applied voltage (under 0.5 mA/cm2) is applied [27]. Iontophoresis-driven Transdermal drug delivery controlled by a smartphone app for managing cancer with medication delivery. Iontophoresis, a form of transdermal drug delivery system utilizing low-intensity electric current, improves drug absorption through the skin for targeted drug delivery and reduced overall side effects. Smartphone-controlled iontophoresis could be beneficial for self-administered cancer treatment [28]. Iontophoresis is an effective method for delivering small molecule chemotherapies because of their small size and stability. Various small molecule chemotherapeutic agents have been tested in both pre-clinical and clinical trials in order to cure basal cell carcinoma, also known as (BCC), and the squamous cell carcinoma (SCC) [29-32].

B. Sonophoresis

Sonophoresis, a technique that utilizes ultrasound enhance the way medications are transmitted through the skin, is being researched regarding its ability to enhance cancer therapies. Recent research is centered on the utilization of sonophoresis to administer drugs like cisplatin in cancer treatment models, such as in cervical cancer xenografts. The objective is to enhance the concentration of drugs within tumors locally while reducing overall toxicity, a critical issue in chemotherapy [33-34].

C. Electroporation

Using high-voltage electric pulses (between 5 and 500 V) for a microsecond to millisecond duration, an electroporation is an innovative physical approach that transports medicinal products into cells and tissues [35]. Electrochemotherapy (ECT) is a newly developed technique that allows for effective treatment options. Electrochemotherapy involves applying electric pulses directly to tumor cells and simultaneously delivering anticancer drugs like cisplatin

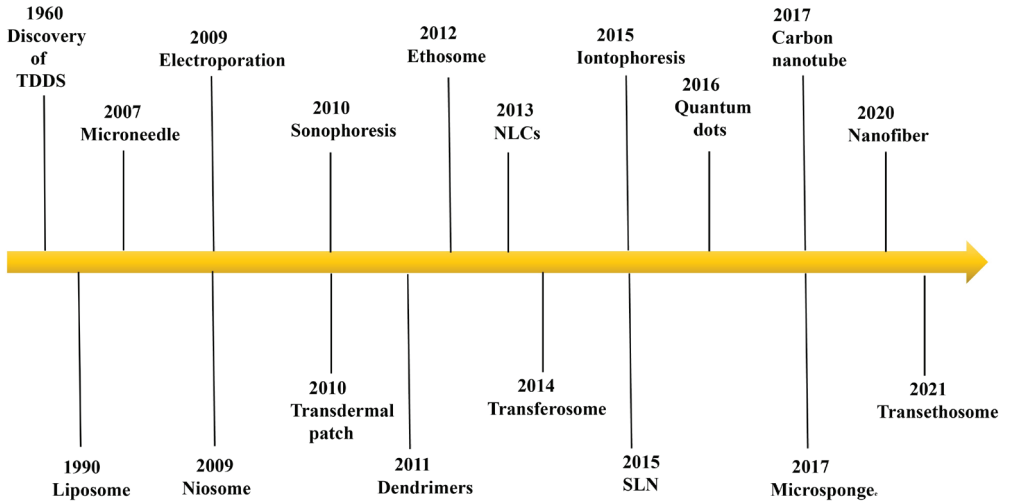

Figure 1. Historical timeline of transdermal drug administration methods for cancer therapy

or bleomycin, either through the bloodstream or directly into the tumor [36].

1.3.2. Mechanical methods

A. Transdermal patch

Transdermal drug delivery adopts the idea of incorporating medications into a "patch" that could potentially be utilized for transdermal administration of various medicinal treatments. Scientists have investigated non-intrusive transdermal delivery, which provides numerous benefits like minimizing systemic damage and preventing the first-pass metabolism [37]. Polymeric patches utilize biocompatible and biodegradable polymers to facilitate controlled or continuous drug delivery [38]. In addition, hydrogel patches, because of their high-water content, which improves skin hydration, and provide comfort or flexibility, which could help increase the absorption of certain medications by causing corneocytes to swell. A new plan was created to address the difficulties of administering doxorubicin (DOX) for treating breast cancer [39].

B. Microneedle

Microneedles, also known as MNs, are minuscule needle-like formations utilized for delivering drugs across the skin's layers. They do not require surgery and are linked to much less or no discomfort at the area where they are applied to the skin. Polymeric microneedle arrays offer a more effective approach for delivering drugs through the skin barrier of stratum corneum with very little invasiveness [40]. Bhatnagar and co-workers discussed the utilization of zein-derived micelles for the administration of tamoxifen and gemcitabine, drugs employed for breast cancer therapy. Various types of microneedles include coated, solid, dissolvable, swellable, and hollow microneedles.

1.3.3. Various vesicular approaches of transdermal drug delivery systems

A. Liposome, proliposome

Liposomes are the most widely used vesicular approach for targeted medication administration, aiming to achieve improved drug efficacy and minimal side effects [41]. Research on liposomal nanomedicine for treating cancer is quickly growing, creating new possibilities for cancer therapy. Liposomal nanomedicine has significant potential in cancer therapy by targeting drug delivery to enhance treatment effectiveness and minimize harm to healthy tissues and cells. Proliposomes are a novel type of medication distribution system that provides multiple benefits compared to conventional liposomes. Traditional liposomes can easily undergo oxidation or hydrolysis, along with sedimentation, aggregation, or fusion with other compounds. However, proliposomes exhibit greater stability compared to liposomes, making them more appropriate for drug delivery [42]. Higher efficacy against drug-resistant (MCF-7/Adr)

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and drug-sensitive (MCF-7) cancers was achieved by combining resveratrol and paclitaxel in PEGylated liposomes [43].

B. Niosomes, proniosome

Non-ionic surfactant created niosomes are small vesicles that enclose solute(s) in an aqueous solution with a membrane made up of non-ionic surfactant molecules in bilayers, either multilamellar or unilamellar [44,45]. Tamoxifen (TMX)/curcumin combination and curcumin alone. Niosomes employ diverse release mechanisms within cancer tissues or cells [46]. The research effectively created hyaluronic acid-coated 5-FU niosomal vesicles that improve skin retention and enable controlled drug release, presenting a promising transdermal method for targeted skin cancer treatment with lowered systemic toxicity. Proniosomes outperform other types of vesicular carriers. Proniosomes are dehydrated formulations of carrier systems covered with water soluble nonionic surfactant that quickly transform into niosomes once hydrated. They are able to address the stability issues commonly found in niosomes and liposomes and can enhance the solubility, bioavailability, and absorption of different medications [47,48].

C. Transferosomes

Liposomes with the ability to change form and flexibility are called transferosomes. The complex system known as a transferosome is extremely flexible, sensitive to stress, and ultradeformable due to its watery core encased in a composite lipid bilayer. The flexibility of transferosome membranes is attained through the addition of appropriate surface-active agents in the correct proportions [49,50]. When transferosomes are applied on healthy skin, they are able to pass through the epidermal cells and intercellular space as they move deeper into the skin under an osmotic gradient [51]. 5-fluorouracil (5-FU) is frequently utilized to treat actinic keratosis or nonmelanoma skin cancer. However, its anticancer potency decreases when applied topically due to limited transdermal penetration [52].

D. Ethosome, transethosome

Ethosomes, a new lipid carrier, have been created with enhanced flexibility and reduced size by incorporating ethanol. It is thought that phospholipids and a high ethanol content work together to promote ethosome penetration into inner skin layers with enhanced skin immersion and potent anticancer efficacity, the mitoxantrone

(MTO) ethosome gel offers a promising non-invasive transdermal approach for carcinoma treatment. [53]. Transethosomes are a blend of transferosomes and ethosomes. Transferosomes can deform and penetrate the skin [54,55]. Transethosomes are innovative, highly deformable vesicles capable of transporting medications into deeper tissues. Transethosomes are made up of surfactants, Phospholipid and ethanol. Every component plays a vital function in the characteristics of the carrier [56].

E. Cubosomes

Cancer is the hallmark as the aberrant and unregulated growth of cells. Various kinds of nanocarriers are currently being examined potential purpose of cancer therapy, which are nano-sized dispersions have caught the interest of researchers as one of various nanocarriers. Cubosomes are colloidal dispersions with cubic crystalline liquid structures in water, aided by appropriate surfactants. Their ability to contain lipophilic, hydrophilic, and amphiphilic compounds within their structure sets them apart from other substances [57]. Recently, a small number of anticancer medications have been successfully enclosed in cubosomes and examined for their physical and chemical properties [58].

1.3.4 Various nanoparticulate system of transdermal drug delivery systems

A. Solid lipid nanocarrier, nanostructure lipid carrier

Solid lipid nanoparticles (SLNs) are crucial nanoscale that have several applications, including the administration of drugs, clinical medicine, or cancer treatment. In the domain of cancer therapy, SLNs are now being recognized as potential nanocarriers to address biological obstacles and resistance to multiple drugs [59]. SLNs have the capability to address current limitations of chemotherapy and challenges associated with traditional chemotherapy and MDR in treating breast cancer. Topical formulations using Nanostructure lipid carrier (NLCs) lead to enhanced cutaneous absorption or extended medication release, resulting in reduced systemic adverse effects or skin irritation. NLCs improve drug delivery by increasing skin permeation due to their smaller size. NLC offers

stability and safeguards for a drug molecule as well. Increased NLC penetration into the skin leads to a gradual release of drugs, resulting in a longer-lasting effect with less frequent use [60].

B. Dendrimers

Another option for using dendrimers as carriers for anticancer drugs is to take advantage of their precise multivalent structure by chemically linking drug molecules to the outer layer. The tuning of the release of the bioactive substance can be adjusted by utilizing the idea of a site-specific degradable spacer placed between the drug and the outer groups of the dendrimer. Additionally, the amount of drug loaded can be modified by adjusting the number of groups on the dendrimer's outer surface. 5- Fluorouracil (5-FU) exhibits strong anti-cancer effects [61]. There is a hopeful potential for the clinical cancer prevention and treatment of dendrimer formulation. [62]. Dendrimers can be utilized in cancer treatment by targeting tumors with specific light-absorbing molecules that have toxic effects on tumor cells. This type of application of dendrimers is used for photothermal or photodynamic therapy [63].

C. Quantum dots

Quantum dots are tiny light-emitting semiconductor crystals. Ranging from ultraviolet to near infrared wavelengths due to their size variability within the electromagnetic spectrum. Experimental evidence has shown that Quantum dots (QDs) can be used for live visualization of cancerous cells, dual in the lab and in living organisms. Distinct markers for cancer like HER2, PSA, folic acid, and CD44 might be detected Within the tumor surroundings via linking a right immunoglobulin and peptide monoclonal antibody towards Quantum Dots. Furthermore, research suggests that Quantum Dots might be contained in paramagnetic liposomes Accompanied by RGD ligands or utilized for visualizing tumor angiogenesis via MRI [64].

D. Carbon nanotube

Among the fullerenes are carbon nanotubes, with an atom of carbon bonded to one another through hybridization of sp2 orbits [65]. Hybridization of orbits refers to how atoms' orbitals are arranged when forming chemical bonds. Sp3 hybridization is more prevalent in diamond's carbon atom arrangement than sp2 hybridization, as carbyne exhibits sp hybridization [66]. Carbon nanotubes (CNTs) fall into two primary classes: single-walled or multi walled [67]. An increasing number of approaches for the administration of anticancer medications have incorporated nanotechnology for strengthening paclitaxel's therapeutic index, Abraxane® (Abraxis BioScience), a drug that forms nanoparticles or is utilized for the therapy of metastatic breast cancer.

E. Microsponges

Rather than entering the skin's layers, tiny, nonreactive, and indestructible balls known as microsponges get trapped in the skin's folds and gradually release the healing substance through diffusion in a controlled manner specific to the skin's requirements, reducing skin damage. An excessive buildup of medications in the skin layers [68]. Traditional skincare products release a large amount of active ingredients for a brief period. This may result in a pattern of excessive short-term medication followed by insufficient long-term medication [69]. Topical gel containing microsponges of 5- Fluorouracil (5-FU) developed for carcinoma of the skin therapy, offering improved skin absorption and less skin irritation [70].

F. Nanofiber

Nanofibers are created with a high level of medicinal substances to enhance their passage through different layers of skin. Polymeric nanofibers are capable of being used for incorporating both water-soluble and fat-soluble medications. Biopolymer-derived nanofibers have also been investigated for transdermal administration. They have the capacity to regulate the prolonged delivery of therapeutic agents [71]. Rengifo, along with colleagues, developed nanofiber mats made of poly (ethylene oxide)-chitosan containing Dodecyl sulfate or carboxymethyl-hexanoyl pyrazoline-loaded chitosan nanoparticles for the management of skin carcinoma [72]. In (Figure 2) we illustrate the schematic representation of vesicles and nanoparticles.

2. Recent Developments in Transdermal Administration of Drugs Systems for Cancer Therapy

In recent years, an in-depth examination of recent literature on transdermal Providing medications for the cure of malignancies reveals a field filled with new

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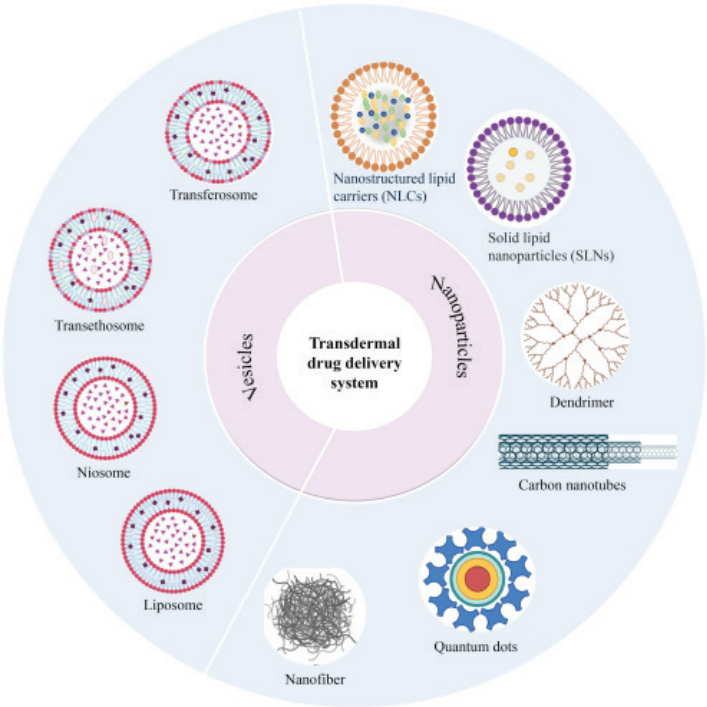

Figure 2. Diagrammatic representations of vesicles and nanoparticles systems

ideas and progress. Here (Table 1) enlist recent advancements done by researchers across the globe to treat different types of cancers by transdermal drug delivery Systems.

2.1. Patented formulations .

(Table 2) include list patented formulations that include recent advancement done by inventos to prepare different forms of transdermal drug delivery systems

3. Application of Transdermal Drug Delivery System for Cancer Treatment

Micro-nanocarriers are often studied in anticancer chemotherapeutics to enhance solubility, achieve regulated release, and boost skin immersion [86,87]. Given that significant adverse effects of chemotherapy, delivering chemotherapy drugs through the skin could be a potential method for enhancing accuracy in targeting localized skin cancers and decreasing overall toxic effects [88]. Jiang and associates created a peptide-based hydrogel to incorporate CPP-modified transfersomes containing paclitaxel for the therapy of skin melanoma [89]. The Enhanced permeability and retention (EPR) effect can be utilized by a well-designed nanoparticle system like Nanostructured lipid carrier for achieving passive targeting of tumors. This way, the previously mentioned challenge of poor tissue specificity can be somewhat addressed. Moreover, advancing in surface engineering skills allows for additional control over the bio distribution of NLC by adjusting their exterior physicochemical properties to target specific tissues [90]. NLCs were employed to enhance the suboptimal pharmacokinetics of the chemotherapy drug included. Dacarbazine is prescribed to treat soft tissue sarcomas, Hodgkin's disease, especially metastatic malignant melanoma [91]. DNA, antisense ODNs, mRNA, siRNA, aptamers, and CpG oligonucleotides are all considered nucleic acid-based therapies [92,93]. Pan and associates created a solution-based MN patch to transmission of siRNA that targets STAT3 for transdermal administration [94]. PEI with a positive charge was utilized to create a compound with STAT3 siRNA, which was then incorporated in the microneedles made of biocompatible HA, dextran, or polyvinyl pyrrolidone. It was demonstrated that MNs could effectively penetrate the skin or quickly dissolve within it [95]. Nano emulsions (NEs) have been thoroughly researched in recent years for their benefits in delivering chemotherapeutic drugs topi-

Table 1. Current Advancement in Transdermal Administration Drug System for the Cancer Therapy.

Systems	Drug used	Cancer type	Outcome of study	References
Solid Dispersion-Loaded Microneedles	Quercetin	Anti-Melanoma Cancer	The optimized Quercetin Solid dispersion-loaded Microneedles inhibited the A375 cells' (melanoma cells') ability to survive by causing cell death	Monsicha Khuanekkaphan et al. 2024[73]
Nanotransferosome	Erlotinib	Ductal Carcinoma	Erlotinib displayed enhanced efficacy against MCF-7 cell lines, lower IC50 values with an enhanced safety profile.	Geeta Aggarwal et al. 2024[74]
Nanofiber	Pistacia lentiscus essential oils and 5Fluorouracil	Melanoma and Breast Cancer	The created 5FU-PLEO-PCL-NFs have the potential to be used locally to treat melanoma and breast cancer tissues (postmastectomy).	Obaydah Abd Alkader Alabrahim et al. 2024 [75]
Transethosome	Glycyrrhizic Acid	Skin Cancer	The produced Glycyrrhizic acid transethosome Based on the data obtained *in vivo,* the formulation was found to be effective in treating skin cancer.	Mohd Aqil et al.2024 [76]
Nanostructured Lipid Carrier	Mannose Conjugated-Doxorubicin-Berberine	Skin Cancer	Ptrepare formulation found with better accumulation and skin penetration compared to traditional skin cancer gel	Sanjula Baboota et al. 2024[77]
Transliposome	Strychnine	Skin Cancer	Transliposome preparation might be a suitable nanocarrier for the cutaneous distribution of Strychnine	Perwez Alam et al.2023 [78]
Transdermal patch	Resveratrol	Breast Cancer	The resveratrol transdermal patches could be a good way to administer medication to specific sites in breast cancer treatment.	Usha Y. Nayaket al.2023 [79]
Aptamer-grafted, cell membrane-coated dendrimer loaded with doxorubicin	Doxorubicin	Triple negative Breast Cancer	While functionalization with aptamers boosted its uptake by cancer cells, covering the RBC membrane on the surface of the dendrimers improved their biocompatibility and blood circulation time.	Prashant Kesharwani et al.2023 [80]
Polyamidoamine dendrimers	Vismodegib	Skin Cancer	The Dendrimer vimodegib Complexes are remarkable nanosystems that may be useful for topical treatment of basal cell cancer.	Fernando C. Alvira et al. 2022 [81]

cally for skin cancer treatment [96]. Nanofiber has been investigated for treating skin cancer due to its ability to offer flexibility in design for functional purposes. Therefore, it dispenses a healing substance at the target location upon interaction with the environment. Janani et al. developed scaffolds made of molybdenum oxide–polycaprolactone nanofiber (MOL–PCL fibers) with nanoparticles incorporated [97]. AuNPs, metallic nanoparticles, have been studied for their potential as drug carriers for delivering the anticancer agent topically. An experiment was conducted to examine how progressively polymer-coated gold nanoparticles (AuNPs) with imatinib mesylate (IM) could treat melanoma. Transdermal delivery provides a great method for introducing immunomodulatory substances into the body [98].

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Table 2. Patented Formulations

Inventor	Patent Number	Title	References
Ryan Beal, Thousand Oaks, CA(US)	US11744853B2	Method of administration and treatment	2023 [82]
Nicholas V. Perricone, Madison, CT (US)	US10155048B2	Methods and systems for treating or preventing cancer	2018 [83]
Audra Lynn Stinchcomb, Lexington, KY (US); Stan Lee Banks, Frankfort, KY (US); Miroslaw Jerzy Golinski, Lexington, KY (US); Jeffery Lynn Howard, Richmond, KY (US); Dana Carmel Hammell, Georgetown, KY (US)	US9533942B2	Use of cannabidol prodrugs in topcal and transidermal administration with microneedles	2017 [84]
Nicholas V. Perricone, Madison, CT (US)	US9795632B2	Cancer treatments and compositions for use there of	2017 [85]

4. Conclusion

The transdermal method of delivering chemotherapeutic drugs is preferred over oral or parenteral routes for various types of cancer due to its benefits. One significant shortcoming of the transdermal method is the complexity in achieving the necessary plasma concentration for therapeutic effectiveness due to low drug permeability through the stratum corneum. Nevertheless, most chemotherapeutic medications are highly potent and work well in small amounts. Hence, developing chemotherapy drugs into transdermal formulations shows great potential. Additionally, certain forms of cancer including breast as well as skin cancers, may be managed by administering medication directly to the impacted regions. This approach focuses on both the tumor and reduces the drug's side effects. The use of iontophoresis for physical enhancement has caused notable changes in clinical practice, particularly in delivering substances quickly and precisely to the skin. Having the capability to electronically regulate delivery rates makes iontophoresis stand out with the potential to be used for patient-controlled dosing and complex delivery profiles. Ultrasound has the potential to enhance transdermal medication by disturbing the stratum corneum on a nanoscale level. The first-generation patch technology will still be utilized for delivering small-molecule drugs, particularly ones that are transitioning from oral or injectable administration due to patent expiration. Vesicular systems are highly beneficial carrier systems across different scientific fields. Vesicular system involves utilizing vesicles like liposomes, niosomes, transferosomes, transethosomes, etc. They are recognized as highly beneficial carrier systems, additives, and tools in different scientific fields. Skin can be disrupted at a microscopic level using advanced techniques like microneedles, thermal ablation, and microdermabrasion. Nanotechnology provides a hopeful approach for accurately aiming at cancer cells while reducing harm to normal tissues. Nanoparticles have the ability to transport therapeutic substances directly to the tumor location, overcoming obstacles presented by the tumor microenvironment. Changes made to the exteriors of nanoparticles can increase their stability, extend their time in circulation, and enhance cellular uptake, ultimately improving their effectiveness. In general, Utilizing developments of both active as well as passive drug transport techniques, the transdermal drug administration approach. We predict that in the future, stimuli-responsive quantum dots and transethosome could be developed to react to environmental triggers like pH, temperature, or tumor-specific enzymes in the microenvironment. This could enable the drugs to be released only at the tumor site, leading to better targeting and less wastage. The Transdermal drug delivery device must include wearable transdermal patches, wearable biosensors, an integrated microcircuit for local processing and storage, and a wireless communication micro-module.

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Conflict of interest

The authors declare no conflict of interest.

Statement of Contribution of Researchers

Concept – B.R., S.G.; Design – B.R., S.G.; Supervision – B.R.; Resources B.R., S.G.; Materials – B.R., S.G.; Data Collection and/or Processing – B.R., S.G.; Analysis and/or Interpretation – B.R., S.G.; Literature Search – B.R., S.G.; Writing – S.G.; Critical Reviews – B.R.

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