IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 3, January 2023

A Thorough Examination of the Nanostructured Lipid Carrier System as a Therapeutic Approach for the Treatment of Skin Cancer

Prakash Maurya[1] and Dr. Dhirendra Babji Sanghai[2]
Research Scholar, Department of Pharmacy[1]
Associate Professor, Department of Pharmacy[2]
Sunrise University, Alwar, Rajasthan, India

Abstract: *When abnormal skin development occurs, it's referred to as skin cancer. Overexposure to sunlight may result in skin cancer, premature aging, and sunburn. We need to be very aware of UV blockers and the best technique to apply them if we want to shield our skin from the sun. The ideal drug delivery technique for topical administration is nanostructured lipid carrier due to its improved solubility, bioavailability, and drug loading capacity. Moreover, they allow a 70% UV blocker to be loaded. The incidence of the condition, its pathophysiology owing to genetic changes in the p53 tumor suppressor gene, the kinds of NLCs and their applications in skin care are all covered in this study. The literature for the research was looked for using Science Direct, Web of Science, Google Scholar, and PubMed. I also used the global Burden of Disease Study database to evaluate the changes in skin cancer globally. Countries differed in the rates at which skin cancers altered. Over this period, there was an increase in squamous cell cancer cases. Males are more prone to get keratinocyte carcinoma, whereas women are more likely to acquire melanoma. Publications have also been made describing several NLC kinds and their defense mechanisms against skin cancer. Highlighting research hotspots pertaining to NLC processes is crucial. Lipid carriers with nanostructures will continue to be developed, resulting in more effective, precise, and safe solutions. The success of nano lipid carriers and the clinical development of NLCs will both benefit from more research. Different demographic groups are disproportionately affected by the incidence and prevalence of skin cancer. Obtaining current data on the incidence of skin cancer and allocating sufficient resources are critical to its elimination.*

Keywords: Nanocarriers, Lipid-based, Skin cancer, Treatment

I. INTRODUCTION

Skin cancer is the term for the aberrant growth of skin cells. Concerns about public health are being raised by the daily increases in skin cancer-related morbidity and mortality rates. Genetic alterations brought on by UV exposure are the main driver of the development of skin cancer. One may reduce their risk of skin cancer by minimizing their sun exposure. Thus, in order to stop skin cancer from spreading, it is essential to fully understand the UVR process (Narayanan et al., 2010). There are three primary types of skin cancer: basal cell carcinoma, squamous cell carcinoma, and melanoma. Chemical carcinogens, ionizing radiation, and environmental pollutants may all cause skin cancer. In addition, age, skin color, diet, smoking, dermatoses, and other types of keratoses, scars, chronic injuries, or non-healing wounds may all contribute to the development of skin cancer (Saladi and Persaud, 2005).

In recent years, pharmaceutical companies have shown an increased interest in nanostructured lipid carriers (Selvamuthukumar et al., 2012). Nanostructured lipid carriers are created by dispersing liquid and solid lipids (oils) in an aqueous solution with a surfactant. NLC has many advantages: They improve the stability of a medicine and its adaptability to different delivery systems. High drug content, low cytotoxicity, and good biocompatibility - preservation methods such as cutaneous, pulmonary, ocular, and intravenous ones.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 3, January 2023

II. BURDEN OF SKIN CANCER

Both non-melanoma and melanoma skin cancers are developing at an increasingly rapid pace. According to Mohan and Chang (2014), basal cell carcinoma is the most prevalent kind of skin cancer. According to Roger et al. (2015), the U.S. diagnoses millions of cases annually. The most common kind of skin cancer is squamous cell carcinoma (Karia et al. 2013). According to Koh et al. (1996), exposure to the sun's damaging UV radiation is a major contributor to the development of non-melanoma skin cancers. In the United States, there will be 87,110 instances of melanoma diagnosed in 2017, with 52,170 cases recorded in males and 34,940 cases reported in women.

About 1% to 2% of skin cancer diagnoses are in India. Although SCC has constantly been cited in many studies from India as the most frequent skin cancer, BCC is also the most common kind of skin cancer in the globe. Despite the lack of accurate incidence data, multiple cancer registries in India revealed that the cumulative incidence of skin cancer ranged from 0.5 to 2 per 100 000 people.

Patients with melanoma were managed based on their recurrence-free survival (RFS) and the length of their follow-up treatments, as well as their age, sex, tissue of origin, location of the illness, number of nodes, lymphadenopathy, and stage of the ulceration. Regional lymphadenopathy and distant metastases were seen in 33% and 32% of patients throughout both treatments, respectively.

Skin lesions and primary tissues from the trunk and extremities showed the greatest frequency of lymphadenopathy. 47% of all treated patients had a full response, 18% had a partial response, and the other patients either had stable illness or a condition that was progressing. In contrast to RFS, where the median was 10, DOFU had a median of 6.2 months. More research is required before a clear approach can be determined for malignant melanoma, according to Sharma et al.

III. SKIN CANCER PATHOGENESIS BY UV RADIATION

Direct cellular damage and altered immunological responses are regarded to be the root of UV radiation's harmful effects on the skin. According to Meeran et al. (2008), UVR damages DNA by producing cyclobutane pyrimidine dimers, oxidative stress, inflammatory responses, mutations in the p53 tumor suppressor gene, and immune system suppression. All of these variables have a significant role in the development of skin cancer. Skin cancer eventually developed as a consequence of dysregulated DNA repair and apoptosis caused by mutated p53 genes. While UVB radiation generates DNA damage and carcinogenesis (Narayan et al., 2010), UVA radiation causes cancer in skin stem cells (Benjamin, 2007).

IV. RATIONALE OF UTILIZING NLC FOR DRUG DELIVERY IN THE TREATMENT OF SKIN CANCER

As seen in Fig. 1, NLCs may be employed as an alternate drug carrier for the delivery of skin cancer medications. The inadequate drainage of interstitial fluid within a tumor is caused by a tumor's faulty, leaky vasculature and poorly developed lymphatic system, both of which are due to improperly controlled tumor angiogenesis. This makes it easier for submicron-sized particles to extravasate and remain in the tumor. The "enhanced permeability and keeping" effect is what is meant by this.

For a well designed nanoparticulate drug delivery device, such as NLC, the EPR effect may help accomplish passive tumor targeting. The distribution of NLC in the body may also be altered to direct them to the tissue of interest by altering the NLC's external physicochemical features (Mehnert and Mäder, 2012). This reduces systemic pharmacological toxicity by increasing the concentration of medication at the tumor sites. NLC doesn't have the high toxicity and acidity as other biodegradable polymeric compounds have. Because of their adaptability as a pharmaceutical carrier, NLCs are a viable method of drug administration for a variety of cytotoxic anticancer drugs.

The relative impermeability of the stratum corneum always serves as a barrier to drug entry through the skin. The formulations should transport the medicine to the action site in a sufficient quantity, which is another issue. Nanoparticulate systems improve medication delivery through the skin and also target the skin's substructures (Majumdar et al., 2019). Due to their nanosize, which allows for direct contact with the SC, nanocarriers may improve the BA of medicines administered topically (Majumdar et al., 2019).

Due to the fact that epidermal lipids are abundant in SC, lipid NPs adhering to the skin surface would enable lipid exchange between SC and the nanocarriers. Drugs may be delivered via the follicles using lipid NPs. Additionally, each

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 3, January 2023

follicle is connected to sebaceous glands that secrete sebum, which enriches the environment with lipids. Lipid nanoparticles may be trapped more easily in this environment. Drug delivery systems designed for cutaneous use have to be non-irritating and biocompatible (Majumdar et al., 2019).

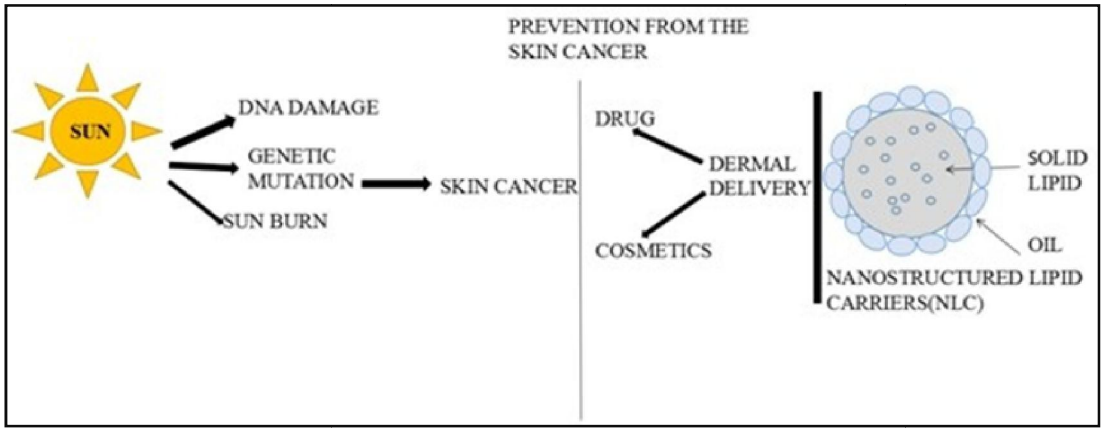

Fig 1: Nanostructured lipid carrier system a promising tool for the treatment of skin cancer.

V. NANOSTRUCTURED LIPID CARRIERS FOR THE TREATMENT OF SKIN CANCER

Oxybenzone, a lipophilic sunscreen found in NLC, is effective at preventing UV-induced erythema and eventually offers protection against UV rays (Table 1).As a result, NLCs were employed as a topical medication delivery method to increase the effectiveness of sunscreens (Gulbake et al., 2012). For the topical application in the treatment of skin cancer, NLCs containing nitrosyl ruthenium complex were produced (Marquele-Oliveira et al., 2010). The antitumor study conducted on an albino mouse skin cancer model showed better prevention of tumor burden in mice, if it is applied to the skin in the form of gel (Iqbal et al., 2019). Silymarin loaded NLC gel prevent from the UV-B induced DNA damage and, ultimately, from skin cancer.

According to Xia et al. (2007), sunscreens incorporated into nanostructured lipid carriers that are employed to filter UV radiations eventually protect against skin cancer. The formulations of newly discovered nanostructured lipid carriers (NLC) (Table 1) that are loaded with octyl p-methoxycinnamate provide an advantageous substitute for traditional sunscreen formulations (do Prado et al., 2020). In order to successfully prevent skin cancer, nanostructured lipid carriers loaded with the antioxidant flavonoid rutin (RT) are used as photoprotective agents (Kamel and Mostafa, 2015). By boosting their deposition in the dermal and epidermal layers, dual medication loaded NLCs were employed to enhance the therapy of skin cancer. According to Imran et al. (2020), quercetin and resveratrol-loaded NLC gel has promise as a treatment for skin cancer (Table 1). Skin cancer is treated with Dacarbazine (Dac), a lipid-soluble and light-sensitive drug licensed by the FDA. Drug release is prolonged and has enhanced solubility thanks to NLC loaded with Dac (Table 1). (2015) Almousallam et al.

The main use of topical photodynamic therapy (PDT) is the treatment of basal-cell carcinoma (BCC), although the main drawback of this method is the insufficient penetration of the photosensitizer. As a result, NLC enriched with 5-amino levulinic acid (5-ALA) have been created to help the photosensitizer penetrate the skin deeply (Table 1). So, according to Qidwai et al. (2016), functions as a potential carrier in the treatment of skin cancer.

Table 1: Different Nanostructured lipid carriers for the treatment of skin cancer

S.No	Drug	Mechanism	References
1.	5-amino levulinic acid (5-ALA)	5-ALA loaded NLC enables the penetration of photosensitizer, consequently increased its cytotoxicity.	Qidwai et al. (2016).
2.	Dacarbazine (Dac)	Dac delivery prevent from the half-life span and low tolerant dose of the drug.	Almousallam et al., (2015

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 3, January 2023

3.	Quercetin and Resveratrol	Quercitin and Resveratrol dual loaded NLC deep penetrate in to the skin	Imran et al., (2020)
4.	Silymarin	Protect from the UV-B induced DNA damage	Iqbal et al., (2019)
5.	Octyl p-methoxycinnamate (OMC)	Octyl p-methoxycinnamate (OMC) loaded NLC inefficient the exposure UV rays in to skin and provide protection against skin cancer	do Prado et al., (2020)
6.	Rutin (RT)	(RT)loaded NLC provide photoprotection ultimately protect against skin cancer	Kamel and Mostafa (2015)
7.	Oxybenzone	Oxybenzone loaded NLC provide protection against UV radiation	Gulbake et al., 2012

VI. CONCLUSION

As standard skin cancer treatment has a number of adverse effects, including severe inflammation, discomfort, a lengthy course of therapy, and unsightly scars on the body. NLCs are the ideal carrier systems and they are effectively sold. NLCs are a new generation of formulations that work better when manufacturing final dosage forms such injectables, creams, tablets, and capsules as well as considerably more flexibility in drug loading and modulating of release. NLC dispersions are very consistent and may be employed in a variety of compositions. According to the extensive literature analysis shown above, NLCs have the potential to be a useful drug delivery system since they increase drug loading, physicochemical stability, drug penetration, solubility, and bioavailability of medicines that are poorly water-soluble while causing little or no skin irritation.

REFERENCES

[1]. Almousallam, M., Moia, C. and Zhu, H., (2015). Development of nanostructured lipid carrier for dacarbazine delivery. International Nano Letters, 5(4), pp.241- 248.

[2]. Benjamin, C.L. and Ananthaswamy, H.N., (2007). P53 and the pathogenesis of skin cancer. Toxicology and applied pharmacology, 224(3), pp.241-248. http://www.cancer.org/acs/groups/content/@editorial/documents/document/ac spc048738.pdfAccessed January 10, 2017.

[3]. Czajkowska-Kośnik, A., Szekalska, M. and Winnicka, K., (2019). Nanostructured lipid carriers: A potential use for skin drug delivery systems. Pharmacological Reports, 71(1), pp.156-166.

[4]. do Prado, A.H., Araújo, V.H.S., Eloy, J.O., Fonseca-Santos, B., Pereira-da-Silva, M.A., Peccinini, R.G. and Chorilli, M., (2020). Synthesis and characterization of nanostructured lipid nanocarriers for enhanced sun protection factor of Octyl p- methoxycinnamate. AAPS PharmSciTech, 21, pp.1-9.

[5]. Gulbake, A., Jain, A. and K Jain, S., (2012). Development of nanostructured lipid carrier as potential sun protectant. Nanoscience& Nanotechnology-Asia, 2(2), pp.210-216.

[6]. Imran, M., Iqubal, M.K., Imtiyaz, K., Saleem, S., Mittal, S., Rizvi, M.M.A., Ali, J. and Baboota, S., (2020). Topical nanostructured lipid carrier gel of quercetin and resveratrol: Formulation, optimization, in vitro and ex vivo study for the treatment of skin cancer. International Journal of Pharmaceutics, 587, 119705.

[7]. Iqbal, B., Ali, J., Ganguli, M., Mishra, S. and Baboota, S., (2019). Silymarin-loaded nanostructured lipid carrier gel for the treatment of skin cancer. Nanomedicine, 14(9), pp.1077-1093.

[8]. Kamel, R. and Mostafa, D.M., (2015). Rutin nanostructured lipid cosmeceutical preparation with sun protective potential. Journal of Photochemistry and Photobiology B: Biology, 153, pp.59-66.

[9]. Karia, P.S., Han, J. and Schmults, C.D., (2013). Cutaneous squamous cell carcinoma: estimated incidence of disease, nodal metastasis, and deaths from disease in the United States, 2012. Journal of the American Academy of Dermatology, 68(6), pp.957-966.

[10]. Koh, H.K., Geller, A.C., Miller, D.R., Grossbart, T.A. and Lew, R.A., (1996). Prevention and early detection strategies for melanoma and skin cancer: current status. Archives of dermatology, 132(4), pp.436-443.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 3, January 2023

[11]. Majumdar, A., Dubey, N. and Dubey, N., (2020). Cisplatin loaded Nano Lipid Carriers for the Treatment of Skin Cancer. Research Journal of Pharmacy and Technology, 13(3), pp.1483-1488.

[12]. Marquele-Oliveira, F., de Almeida Santana, D.C., Taveira, S.F., Vermeulen, D.M., de Oliveira, A.R.M., da Silva, R.S., Lopez, R.F.V., (2010). Development of nitrosyl ruthenium complex-loaded lipid carriers for topical administration: improvement in skin stability and in nitric oxide release by visible light irradiation. Journal of Pharmaceutical and Biomedical Analysis, 53(4), pp.843-851.

[13]. Mahant, S., Rao, R. and Nanda, S., (2018). Nanostructured lipid carriers: Revolutionizing skin care and topical therapeutics. In Design of Nanostructures for Versatile Therapeutic Applications (pp. 97-136). William Andrew Publishing. https://www.mayoclinic.org/diseases-conditions/skin- cancer/symptoms-causes/syc-20377605.

[14]. Mehnert, W., Mäder, K. (2012). Solid Lipid Nanoparticles: production, characterization and applications. Advanced drug delivery reviews, 64, pp.83-101. Mohan, S.V. and Chang, A.L.S., (2014). Advanced basal cell carcinoma: epidemiology and therapeutic innovations. Current dermatology reports, 3(1), pp.40-45.

[15]. Meeran, S.M., Punathil, T. and Katiyar, S.K., (2008). RETRACTED: IL-12 Deficiency Exacerbates Inflammatory Responses in UV-Irradiated Skin and Skin Tumors.

[16]. Narayanan, D.L., Saladi, R.N. and Fox, J.L., (2010). Ultraviolet radiation and skin cancer. International journal of dermatology, 49(9), pp.978-986.

[17]. Rogers, H.W., Weinstock, M.A., Feldman, S.R. and Coldiron, B.M., (2015). Incidence estimate of nonmelanoma skin cancer (keratinocyte carcinomas) in the US population, 2012. JAMA dermatology, 151(10), pp.1081-1086.

[18]. Saladi, R.N. and Persaud, A.N., (2005). The causes of skin cancer: a comprehensive review. Drugs of Today, 41(1), pp.37-54.

[19]. Selvamuthukumar, S. and Velmurugan, R., (2012). Nanostructured lipid carriers: a potential drug carrier for cancer chemotherapy. Lipids in health and disease, 11(1), pp.1-8.

[20]. Sharma, K., Mohanti, B.K. and Rath, G.K., (2009). Malignant melanoma: A retrospective series from a regional cancer center in India. Journal of cancer research and therapeutics, 5(3), p.173.

[21]. Xia, Q., Saupe, A., Müller, R.H. and Souto, E.B., (2007). Nanostructured lipid carriers as novel carrier for sunscreen formulations. International journal of cosmetic science, 29(6), pp.473-482.