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Liposomes Based Approaches for Topical Management Of Burn Therapy

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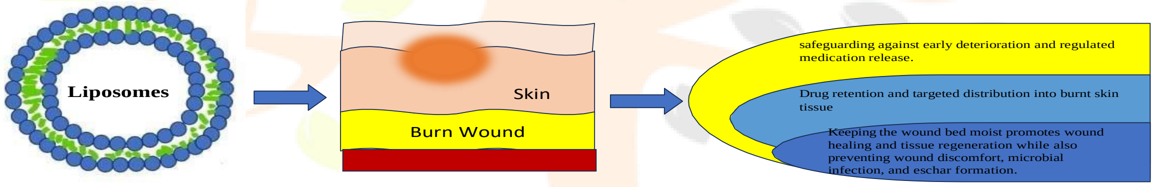
Graphical Abstract



Abstract: The quality of life of an individual may be negatively impacted by burn injuries for a long period, because of the detrimental impact on one's physical and emotional well-being. They will then probably experience psychological issues as well. A key issue is that deep burns heal more slowly than superficial burns, making treatment more difficult and resulting in microbial infection susceptibility. Traditional topical treatments for burns can occasionally be ineffective because they cannot maximize transcutaneous absorption at the site of injury and speed up recovery. Nevertheless, nanotechnology offers a viable path forward for the improvement of current medical wound treatments. It can successfully address issues such as insufficient medication stability, permeability, solubility in water, and bioavailability. This evaluation emphasizes lipid-based vesicles, which serve as an illustration of innovative delivery techniques and highlight their capacity, and therapeutic advantages in the management of burn injuries. Liposomes may aid in removing obstacles such as the limited bioavailability of active medications, provide more controlled drug release, better drug stability, fewer side effects, and less frequent dosing—all of which will eventually boost patient compliance and therapeutic success. since they have better skin penetration than traditional burn topical treatments. The present state and potential applications of these carriers in burn care are addressed here. Additionally, a summary of the burn treatment alternatives that are currently on the market is provided.

Keywords: Burn infection, liposomes, vesicular drug delivery, nitrofurazone, antimicrobial agents

1. INTRODUCTION

1.1 History

Numerous patients have burn wounds that either completely heal or leave scars on a global scale. Treating burn damage has been difficult for researchers because of their inadequate understanding of the condition. The phases of the healing process are critical for the drug delivery employed in healing. Any type of skin injury caused by radiation, heat, electricity, chemicals, or other substances is known as a burn. Both the superficial (papillary) and deep (reticular) layers of the dermis are impacted by second-degree burns. Blisters, agonizing pain, and these sorts of burns result in redness. Burns to the second degree are typically caused by hot liquids and water[1].

The survival rate of individuals with severe burns has increased significantly over time. Modern resuscitation procedures improved dietary requirements, and the advent of novel surgical techniques like cellular treatments have all played a significant role. Prolonged use of a ventilator, an elevated proportion of total body surface area burns extended use of glucocorticoids or antibiotics concurrent degenerative illnesses, or central catheter implantation[2]. For patients with severe burns, all of these raise the risk of bacterial or fungal infection. Therefore, there is an urgent need to develop effective medical practices that promote rapid wound healing and, in particular, to progress topical antifungal medications[3].

Intricate responses to burns are linked to mortality, morbidity, and hypermetabolism. Furthermore, given that burn injuries have a protracted detrimental impact on a person's standard of living and gradually deteriorate both their physical and mental health, they can be among the most catastrophic injuries a person can have. Patients with severe burns may occasionally experience psychological problems. Furthermore, there used to be a relatively high death rate from burn injuries, but in recent decades, improvements in therapy have increased patient survival. Changes in treatment procedures and burn centers have led to this decrease in deaths. However, because burn patient treatment is extremely expensive, the enduring rate of burn patients has put a tremendous financial burden on both the government and patients worldwide[4].

1.2 Physiology of burns

Degree of burns: There are three types of burn injuries worldwide. First-degree burns only cause surface damage to the skin; Second-degree burns also cause damage to the first and second layers of the skin; and third-degree burns cause damage to all layers of the skin. Additionally, the skin is killed by third-degree burning of fat tissue[5]. The table below details burn degree characteristics and management.

Class of the burn	Characteristics	Indications	Supervisory	References
Initialclass	Light burns, which make up less than 10% ofthe body's surface. Being admitted to the hospital is uncommon.	Discomfort, the top layer of skin, epidermis is red. Not a single blister.	Give the burn area fiveto ten minutes of flowing water immersive utilizing Cold Compresses. Aloe vera geland other cooling topicgel. Medicines applied topically such as Bacitracin cream. Medication for pain such as Ibuprofen & Acetaminophen.	[6]
Secondclass	Mild burn It covers about 10% of the surface area of the body. Staying in the hospital may be required.	Pain &redness. Impact the skin outermost layer (dermis) and innermost layer (epidermis). Causing blisters & swelling.	Identical care to thatfor a first-degree burn. Stronger local antibiotics, such as 1%cream Silver sulfadiazine. Treating and bandaging thefractured open	[7]

			burn. Extending limbsto lessen edema.	
Thirdclass	severe burns that encompass more than 10% of the surface of the body. Potentially fatal. Hospitalization is required Recuperation of patients.	Every layer of theskin is affected. Skin color; black brown, yellow, or white. Bloating. Dry &leathery skin. Because of the damaged nerve ending thereis no pain.	Eliminating damaged skin and dead tissue from the burnt area. Excessive replenishment of Fluids (IVmixed fluids /to prevent hypovolemic shock& dehydration. Antibiotics are used intravenously and orally to avoid infection and septicemia. Topical antibiotic creams or ointments. A humid, heated atmosphere for the burn. A diet heavy in protein. Vitamins & minerals tetanus vaccination. Both functional and aesthetically pleasing rebuilding. Through skin grafts damaged tissues are replaced with healthy skin generated from	[8]

			other body parts that are afflicted. A temporary supply of skin transplants from donors or synthetic skin grafts can be obtained.	

1.3 Microbiology of burn infection

The microbial species is accountable for the infection of invasive burn wounds. Among these species, antibiotic resistance is prevalent[9]. There are specific guidelines on the differentiation between colonization (which occurs in almost all burns) and infection (which is likely to result in disease) in burn wounds[10]. Invasive" microbial infections are the most dangerous. The microbiological species that inhibit or infect burns follow a reasonably predictable time pattern [11]. Within the first 48 hours, these bacteria include Staphylococci. burns eventually become colonized with more bacteria, either from the hospital environment or from the host's natural upper respiratory and gastrointestinal flora, after an average of 5-7 days.[12]

1.4 Physiology of Burn Infection

Patients are more susceptible to infection due to many physiological characteristics of the burn surroundings, which reduces the effectiveness of systemic antibiotic treatment. Due to heat damage, the burned area is regarded as non-vascularized tissue as the microvascular system breaks down... Burns upregulate the processes of proteolysis and lipolysis[13]. One major factor that predisposes burn patients to infection is immunosuppression. Immunosuppression involves the immune systems, both innate and adaptive. Many of these require at least three to five days to manifest, to be selectively activated by specific antigens to grow clonally. After thermal injury, the innate immune system changes, affecting NK cells, neutrophils, macrophages, monocytes, basophils, NK cells, complement, and so on. On the other hand, heat injury is linked to numerous mediators that come from the endocrine system, the cytokine network, and the arachidonic acid cascade, which all work together to inhibit the immune system[14]. Sepsis is more likely to occur when bacterial translocation, a physiological reaction triggered by both burns and microbial infection, occurs[15].

2. Drug delivery Systems for Vesicular Drug Delivery

The main issue with topical treatments nowadays is that most drugs only partially pass through the skin because of the barrier function of the skin. Consequently, researchers have put forth innovative formulation methods to enhance burn treatment efficacy and profound skin penetration. Among these methods is the integration of drug molecules into vesicular lipid delivery systems. These delivery mechanisms are carried by cubosomes, ethosomes, liposomes, niosomes, and transfersomes, among other systems[16].

2.1 Liposomes for Vesicular Drug Delivery

Liposomes are globular encapsulations that have one or additional concentric phospholipid bilayers encircling an aqueous center. Due to their numerous benefits, liposomes have been researched as a possible drug delivery system. Since 1970: they can contain both active medicinal ingredients that are hydrophilic and hydrophobic and they can lower the risk of toxic drugs like chemotherapeutics causing severe side effects [17]. They can control drug release patterns over a long period and they can reduce dosage frequency, which increases patient compliance [18]. As a drug carrier system, liposomes can provide a regulated and extended release of a treatment given topically. In the pharmacotherapeutic domains, liposomes have been employed to enhance the efficacy of therapeutic medication administered by oral, topical,parenteral, ophthalmic, and routes.

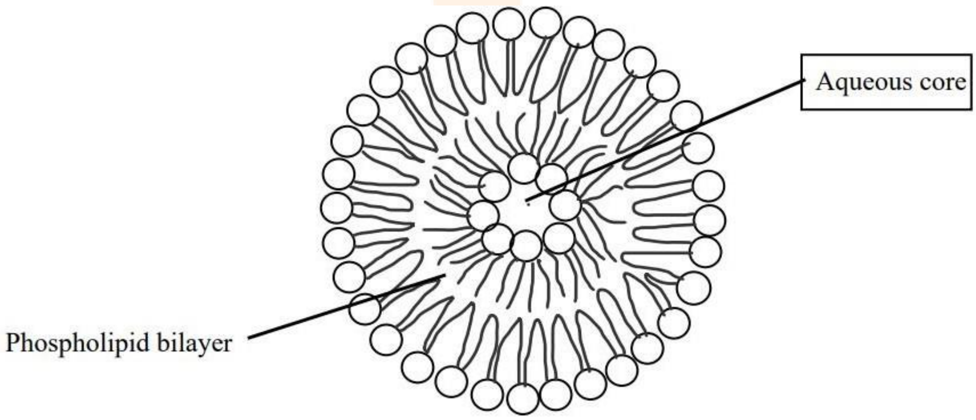
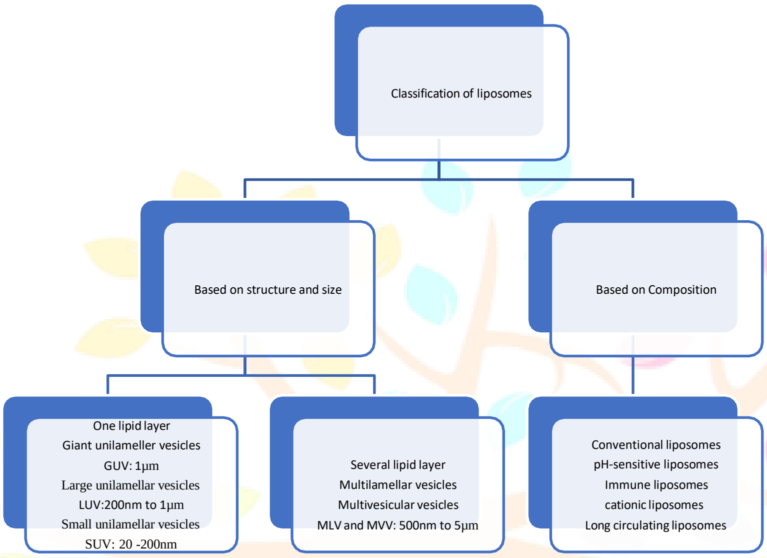


Fig . Liposome

2.2 Physicochemical properties of liposome: The physical characteristics of liposomes, including their number of lamellae, surface charge, rigidity or flexibility of the membrane, lipid content, and possibilities for drug storage [19], ascertain their medication delivery and stability.

Classification of liposomes



2.3 Mechanism of liposomes

The benefits and downsides of liposome drug carriers largely depend on how liposomes interact with cells and what happens to them in vivo after delivery[20]. The liposome's ability to combine with the plasma membrane of cells by simultaneously releasing its liposomal contents within the cytoplasm and introducing its lipid bilayer into the membrane is incredibly rare. The replacement of bilayer constituents with components of cell membranes, including cholesterol and lipids. It's common for multiple mechanisms to operate at different times, and it can often be challenging to determine which one is in use [21 22].

2.4 Topical efficacy

- The recommended course of action is determined by the burn's location and the skin'sability to penetrate it.

- Excellent effectiveness in treating dermatitis, psoriasis, and wound infections, amongother skin conditions.
- To enhance its transdermal penetration and wound-healing properties, liposomalformulations for film dispersion were created[23]

2.5 Advantages of liposomes

- Liposomes improve the therapeutic index as well as the efficacy of the drug(actinomycin-D).
- The stability of the drug was enhanced by encapsulation into liposomes.
- Liposomes can be delivered systemically or non- systemically and are non-harmful,adaptable,

biocomptable, degradable in nature , and non- immunogenic.

- Liposomes lessen the toxicity of the contained drug (Amphotericin B, Taxol).
- Liposomes minimize the quantity of medication that gets into sensitive areas of thebody.
- Adaptability to combine with ligands unique to certain sites to produce activeTarget[24].

3. Nitrofurazone

Nitrofurazone is an antibiotic belonging to the 5-nitrofuran class. The presence of a 5- nitrofuran ring sets apart the broad-spectrum antibiotics in the nitrofurazone family, which are efficient against microorganisms classified as gram-positive and gram- negative. Topical nitrofurazone formulations are used to treat burn infections and prevent bacterial infections in burn victims. Second-degree burn treatment uses facilitates this[25].

4. Preparation method of liposomes.

4.1. Dry film method

The dry film approach was used to make liposomes. For the manufacture, three distinct lipid compositions were utilized: PC, pc/PG (1/9, molar ratio), and PC/SA(9/3, molar ratio (Pavelic et al., 2005) [26]. To summarize, a Buchi R-124 rotary vacuum evaporate was used to extract the solvent after the lipid components had been dissolved in the methanol (26mmol/1). After being manually shaken for five minutes, the lipid film was rehydrated in ten milliliters of pH

6.7 distilled water. Before being further defined and sized down, the liposome suspension wasrefrigerated for the entire night [27].

4.2. Sonication method

Liposomal suspensions of various sizes were prepared using a cole parmer ultrasonic processor. After cooling in an ice bath, the liposomal suspensions underwent three rounds of continuous cycle sonication at 40% amplitude for 20 seconds each[28].

4.3. Solvent injection method

In summary, a heating magnetic stirrer was used to dissolve 1 ml of propylene glycol and 40 mg pc 4% w/v at 47 c for 15 minutes at 750 rpm. 40 mg of the medicine was dissolved in 9 ml of PBS buffer (5.8 p.H 0.1 M). In streamlined flow, the medication solution was added over 30 to 35 minutes at 750 rpm and 55 to 60 degrees Celsius using a peristaltic pump connected to a syringe. The container was properly sealed with a cork and parafilm. Using a microprobe sonicator, the resulting dispersion was sonicated for 20 minutes to obtain the final liposome formulation. Following placement of the liposomes atop the G-50 column, they were spun at 3000 for 20 minutes at room temperature (four degrees Celsius), the medicine that had been released from its entrapment finally settled at the bottom of the centrifuge tube, where it was collected and lyophilized[29].

5. Characterization of liposomes

5.1 Size reduction

A sonics High Ultrasonic processor was used to sonify liposomes to reduce their initial size. Five 2-minute cycles of the 40 W sonication were performed, separated by a 2-minute rest period[30]. The sample was submerged in an ice bath to prevent heating up. Later, the diameters of the liposomes were examined using dynamic light scattering. The initial liposome size was reduced. Five cycles of two minutes each were performed at 40 W, with two minutes off in between[31 32].

5.2 Size distribution of liposomes

The liposome mean diameters were characterized using two different techniques: dynamic light scattering and flow cytometry. To ascertain the initial size of the produced vesicles, flow cytometry analysis was performed on the liposomes synthesized with different dispersion phases[32]. 400 milliliters was the limit volume and 106 events was the analytical limit. The size distribution and evolution of the liposomes were measured after preparation and after 7,14,21, and 28 days of storage. Dynamic light scattering was used to examine the liposomes prepared with various dispersing phases, such as PBS and Nacl [33].

6. Evaluation of liposomes

6.1 Drug entrapment efficiency

The entrapped medication was extracted from liposomes using dialysis tubing to assess the entrapment efficiency of mupirocin, Usually, 5milliliters of liposomal solution were dialyzed against 1000millilitres of water for the duration of the dialysis to guarantee skin conditions. The entrapment efficiency was calculated using the formula [(T-C/] × 100, where T is the total quantity of drug included in the sample and C is the amount of free drug present in the water after liposomal dispersions were dissolved in methanol. The drug recoveries for each sample were computed [34 35]

6.2 Particle size

With the help of a microscope, the kind of liposomes was determined as MLA. A laser was used to assess the liposome particle size. The mean particle size of the liposomes was found to be 4.44± 0.03 µm using a diffraction particle sizer[36].

6.3 Stability

Under urgent conditions, the liposome suspension stability was examined. Samples were stored for 30 days at 40ºC in sealed vials. By using dynamic light scattering to measure the vesicle size and size distribution[37 38]. In stability testing at 4-8ºC for cold storage, an accelerated stability test was carried out to assess the vesicle's stability. After being chilled for 48 hours, none of the samples exhibited any indications of drug precipitation. Sonicated vesicles, on the other hand, very slightly raised the polydispersity index from 0.36 to 0.39 while increasing the mean diameter in accelerated stability tests by 15% - 20% of the initial size. It was demonstrated that vesicles prefer to assemble under pressures, such as at 40ºC [39].

7. Current Burn care practices used locally

Treatment for burn injuries includes topical antimicrobial dressing changes regularly along with debridement and cleaning. It's debatable which antimicrobials or dressings work best for controlling or preventing infection or accelerating wound healing. Topical therapies are primarily intended to facilitate wound healing and maintain the cleanliness of the burn site [40]. Topical therapy offers a high patient compliance rate, is noninvasive, and can be removed from the skin after usage. This is because it enables the delivery of medication straight to the site of injury, increasing therapeutic eff, decreasing undesirable adverse effects, and relieving the difficulties related to burn injuries. However, the main issue with current topical treatments is that, because of the skin barrier function, the majority of drugs only partially permeate the skin

[41]. For this reason, topical treatments should be used in conjunction with adequate basic wound care.

Based on the stage and degree of burn severity, topical medications, and dressings are utilized to treat it. Additional aspects, such as wound quality and status, patient skin allergies, therapy availability and cost, and patient desire[42], must be taken into account to choose the best course of action. At present hospitals and pharmacies offer three local burn wound therapies;
(a) biological graft; (b) semi-biological skin substitutes; and (C) standard topical antimicrobial drugs, which include cleaners, ointments, dressing, and creams. It is clear that because of their limited ability to penetrate the epidermis, current antimicrobial drugs are not suitable for treating serious burns. They also have major drawbacks and additional restrictions[43].

7.1 Topical antibiotics

Strong topical antibiotics were frequently applied, which reduced the microbiological load and risk of infection on the burn wound surface [44,45] The drug ability should be the primary consideration when choosing a topical antibacterial therapy to kill bacteria collected from burn wound surveillance cultures. As evidenced by current patents, these compounds may find application in dressings of wounds, bio-membranes, and wrapping around materials, in addition to postoperative adherent and cosmetic materials. To mitigate the development of antibiotic resistance, burn units may choose to alternate between applying multiple topical antibacterial therapies [46,47]

Example of topical antibiotics for burn wound healing

7.1.1 Mafenide Acetate: Topical Mafenide acetate 0.5% cream, often known as Mafenide, contains Sulfonamide molecules. It can be administrated without a covering; it facilitates routine surface examination of the burn wound and open burn wound treatment. [48] Before the development of Silver Sulfadiazine, Mafenide was a frequently prescribed drug for burn treatment. Dressings made of gauze must be saturated with a 5% solution. It works just as well in this way as the cream preparation [49]. Due to its restricted efficacy, this medication ought to be taken along with Nystatin to avoid activity against fungi [50]. The usage of Mafenide acetate across wide surface dimensions of this substance can be lethal in burn patients with simultaneous respiratory acidosis [51]

7.1.2 Bacitracin: The isolation of these organisms was first reported in 1945[52]. Tracy generated a mixture of similar cyclic polypeptides known as Bisitracin. Topically applying Bacitracin zinc at concentrations between approximately 5% and 8% helps encourage regenerative healing in wounds. It is optimal to permeate the Bacitracin zinc in an absorbent pad [53] whether used in a hydrophilic or hydrophobic carrier.

7.1.3 Mupirocin: Staphylococcus aureus and coagulase-negative Staphylococci are among the gram-positive topical flora that are effectively inhibited by Mupirocin [55,56], generated during the metabolizing process of Pseudomonas luminescens. Prescription medication formulations containing Mupirocin and Chlorhexidine are helpful in the management of bacterial infections of the skin, particularly infected burns [57]. Mupirocin is also being appliedtopically for burn injuries.[58,59]

7.1.4 Neosporin: Neosporin is a broad-spectrum antibiotic ointment based on petroleum jelly that contains three different antibiotics. Drawing from a qualitative examination of a research study comprising participants with superficial burn injuries, Staphylococcus aureus, and Pseudomonas sp were the most frequently detected invasive bacteria. In many cases, healing took up to 15 days; however, PVP + N also sped up healing times. Still, there was minimal difference in the death rates between the two cohorts of [60].

7.1.5 Nitrofurazone: Nitrofurazone is a topical anti-infective drug, a potent tool against Gram- positive and Gram-negative bacteria. Overall, patients treated with Nitrofurazone cream responded well to treatment for invasive Nitrobacteria cloacae burn wound sepsis. 66% survival compared to the 86% death rate stated in the works of literature[61]. A catheter coated with Nitrofurazone was developed specifically for burn patients [62]. For burn patients, using these catheters may be crucial to reducing their chance of developing a urinary tract infection. Nitrofurans have shown efficaciousness against species that have acquired resistance to antibacterials, despite mounting worries about bacterial resistance to several anti-infective treatments[63].

7.1.6 Silver Sulfadiazine: The reason for the sudden spike in interest in silver is the rapid growth in resistance of microorganisms. In 1970, Fox[64], combined Sodium sulfadiazine (SSD) and Silver nitrate. The antibacterial qualities of Sulphadiazine and the inhibitory impact of silver are combined to create Silver sulfadiazine[65]. Silver sulfadiazine, which was first created as an ointment, was afterward combined to create a cream with a hydrophilic texture[66]. According to recent studies, SSD may prevent wounds from healing. Cho Lee et al.,[67] suggested that growth factor on the epidermis (EGF) would considerably mitigate the detrimental impact of SSD on the healing of wounds, which would ultimately lead to the possibility of SSD incorporating EGF into future designs. The issue of bacterial resistance to Sulphadiazine [68] is an additional concern. There have been reports of SSD-resistant Pseudomonas species; to treat these species, a patent was obtained for a formulation that combines SSD with Sodium piperacillin, which is highly effective against Pseudomonas [69]. Several other patents have been granted for different SSD administration methods, such as topical spray preparations [70], water-dispersible hydrophilic carriers[71], and animal tissue dressings[72].

Some of the currently available, marketed topical antibiotic treatments for burninjuries [73]

Antimicrobial agents & Branded names	**Dosage form**	**Clinical Indication**	**Side effect**	**Contraindications**
Mupirocin Bactroban, centany .	Ointment , cream (2%)	Perineum, face, and burns on a small to medium surfacearea. a substitute in the event of a sulfonamide allergy.	Increased yeastand skin sensitivity.	Allergy responseand bacterial resistance.
Sliver sulfadiazine (1%), in cream form, sulfadiazine, thermazene, and SSD cream.	Cream (1%)	Any kind of burn (with little, medium, and big sections of the wound exposed).	Leukopenia, neutropenia, and skin allergies.	Allergies to sulfonamides, newborns, nursing mothers, and pregnant women.
Bacitracin Mycitracin, Neosporin,Triple antibiotic.	500 IU/g of ointment	Injuries to the face, perineum, and graft sites caused by burnsof all sizes. A choice in case of allergyto sulfonamides.	Growth of yeastand skin allergies.	Allergic response, bacterial resistance, and reepithelialization indicators.
Mafenide Sulfamylon.	Cream(8.5%) Solution(5%)	Burn marks on the nose, ears, and small area of the wound.	Inhibition of pain, metabolicacidosis, and regrowth of the epithelium.	Substantial burn area (more than 40% of the Bodysurface area); sulfonamide hypersensitivity.

Chlorhexidine Betasept, Bipotch, Calgon Vesta, Dyna-Hex, Hibiclens.	Cleanser forthe skin	Burns only onthe surface.	Hypersensitivityof the skin	Severe burns ordeep burns.
Bismuth–impregnated petroleum gauze Xeroform petrolatum dressing.	Adornments	favored attirefor skin graft recipient sitesand pediatric applications.	There are noside effects mentioned.	allergic responses.
Nanocrystalline silver Nanomac Silver Gel.	Dressing	All burn sizes (medium, large, and tiny wound surface areas).	systemic absorption of silver and skin discoloration.	Burns around the eyes, pregnancy, and silver allergy.

9. Burn treatment applications for liposome-based formulations

Drug	**Therapeutic action**	**Prefabricated Formulation**	**Model used**	**Results**	**Reference**
Amphotericin B	Burn victims' preferred broad-spectrum antifungalagent	Commercial products that include Amphotericin B liposomal in experiments	*In vitro*	In opposition to Aspergillus, liposomal Amphotericin B has demonstrated exceptional antibacterial effectiveness *In vitro*.	[74]
Silver sulfadiazine	Cures and prevents second and third-degree burn & wound infections.	A topical dressing containing silversulfadiazine encapsulated in a liposome.	Rats were sacrificed, and P. aeruginosa colony- forming unitswere injectedinto the	A single administration of antibiotics entrapped in liposomal membranes produced a beneficial	[75]

			muscle and rat tissue.	outcome. It would typically call for severaldoses of traditional treatment.	
Epidermal growth factor	EGF promotes epidermal and dermal regenerationto improve wound healing. encouraging the developmentof cells.	EGF-loaded liposomes in gel formulations made of chitosan.	Rats	Rats were used inan experiment tolook into how formulations affected healingin second-class burn injuries. The liposomal gel formulations including EGF based on the histochemical data, had the highest rate of epithelialization.	[76]
Bupivacaine	Analgesia following surgery	Liposomes filled with bupivacaine.	An investigation in burn patients.	Postsurgical analgesia was induced by the administration (autograft harvesting) at the surgical site in the burn patient.	[77]

10. Current Situation in Burn Therapy and Concepts for the Future

Liposomes have the potential to carry biological pharmaceuticals that are made up of macromolecules including recombinant proteins, antisense oligonucleotides, and cloned genes[78]. These liposomes can also be changed and carefully constructed to achieve enhanced drug delivery through various routes of administration. Nevertheless, there aren't many of this kind in the pharmaceutical market; the challenges of producing liposome-based medications on a big scale have made them scarce. Liposomal Histx (Quali®-C), for example, is an oral suspension dietary supplement made by Equisalud that contains vitamin C and Quercetin [79]. According to earlier studies, Vitamin C is a good antioxidant choice for burn patients since it effectively reduces the need for fluid and breathing during the first stages of the burn infection. In the burn wound stasis area, Quercetin improves tissue viability by reducing apoptosis and increasing autophagy[80]. Enhancing the bioavailability and effectiveness of these supplements is the primary goal of employing liposome lipid carriers [81]. Nutricology®, Micro Liposomal C, is an additional illustration of cutting-edge vitamin C nutrition [82]. However, topical liposome preparation has been created and is applied to the treatment of burns and other skin injuries. Among these is the Serum for Advanced Repair with Decorté® Liposomes. Liposomes power this topical serum, which provides long-lasting skin hydration and support technology[83]. It reduces the skin's infection and elastance and greatly increases its distensibility[84]. Furthermore, because sterols are included in the liposome's constituent parts, liposomes are a useful tool for protecting retinol against light-induced oxidation. Due to the great augmentation of drug penetration into the deep skin layer by the deformable liposomes, the combination was considered promising for the management of burn wounds with deep, partial thickness [85].

11. Some Patents on Liposomes used in burn treatment

Number of patents	Origin	Title to patent	Spheres	Date of publication	Reference
US7476400B2	China	High-concentration lidocaine composition and preparation techniques	Liposomes	13 January 2009	[86]
KR100446832B1	South Korea	Droplets of liquid used inthe production of preparation for the non-invasive passage ofactive substances through obstacles	Liposomes	4 September 2004	[87]
US20200276231A1	United State	Improved antivirulence for microorganisms resistant to antibiotics	Liposomes	3 September 2020	[88]

12. Conversation and Professional Judgement

The first, second, and third phases of burns are distinguished by differences in the extent, depth, and symptoms of the burned skin, as has been previously stated. As a result, burn treatment can involve everything from skin grafting and surgery to skin cooling and straightforward topical antibiotic therapy. Third-degree burns are thought to be the most serious kind and can lead to a variety of health issues [89]. However, when properly cared for with wound dressings and other topical therapies, burns that are superficial can mend swiftly, and painlessly, along with minimal chance of scarring. At the moment, the majority of burn treatments that are sold commercially are topically applied and traditional. These topical medicines are frequently utilized in the different stages of mild to moderate burn treatment and a variety of pharmaceutical dose forms, including ointments, creams, gels, and dressings. This is a result of topical dose forms' non-invasiveness and high patient compliance due to their ease of application and removal by the injured. Furthermore, topical medication delivery is useful in treating a range of skin conditions, such as acne, microbial infections, and psoriasis[90].
One of these attempts is medication loading to lipid-based vesicles. It has been demonstrated by earlier studies that packing drugs into these lipid carriers can greatly enhance their deep skin absorption and diffusion, resulting in increased skin-healing efficacy. However, systemic antibiotics may be required at high dosages for burn therapy, which can result in the development of antibiotic resistance. Although topical antibiotics or antiseptics do not lead to resistance, they are effective but have several negative effects[91]. To prevent and/or treat burn infections, a wide range of topical antimicrobial medicines have been approved, investigated, or suggested.

The research on cutting-edge burn treatments that use liposome-based medication delivery systems and their many benefits, is carefully reviewed in the present investigation. Additionally, readers will obtain an improved grasp of the various burn phases and how to cure them. Consequently, we have offered a comprehensive analysis of prospective advancements for topical formulations of burn care treatments.

To prevent and treat burn infections, a wide range of topical antimicrobial medicines have been approved, investigated, or suggested. Burn pathophysiology indicates susceptibility to contagion from a range of bacteria, and empirical evidence suggests that current treatments outperform systemic antibiotics in terms of clinical success. Furthermore, the growing prevalence of multidrug resistance emphasizes the significance of safe and efficient topical treatments.

13. Conclusion

Burn injuries are harmful to both physical and mental health, as they can negatively impact someone's standard of living. Additionally, treating burns presents several difficulties, particularly when it comes to burn injuries and scarring from burns of the second and third degree. They necessitate intensive surgical care as well as tissue and cell culture reconstruction. For those with serious burns, topical liposomal administration may be an option. characteristics include improved drug stability, easier application over wide surfaces, less systemic toxicity, increased penetration, and localized antibacterial action.

As liposomes can regulate medication release, improve drug stability, and raise the solubility of poorly soluble pharmaceutical ingredients, they are at the forefront of cutting-edge techniques resulting in skin regeneration and burn healing increase patient compliance, and provide greater efficacy with fewer adverse effects. However, the creation of such formulations necessitates a thorough comprehension of the both chemical and physical characteristics of the excipients, and active components, manufacturing hydrophobic and hydrophilic medicines more effectively, and offering a plurality of techniques for administration. liposomes have the potential to allow a regulated and prolonged release of the medication of drugs applied on the skin. Nevertheless, an effective topical delivery system for antibiotics intended for burn therapy.

Liposomes are a desirable medication delivery method due to their broad range of applications administered by several routes and have been utilized to deliver a variety of drug modalities. They are suitable for excipient compositions and chemical alterations. Since the discovery of liposomes, new lipid constituents, and preparation techniques have led to a major modification in the technology used in their creation. The clinical needs of liposome-based treatment have not yet been satisfied, even though there are numerous FDA-approved liposome-based drugs on the market and others that are actively being developed. Batch repeatability, minimal entrapment in some drug candidates, efficient sterilization techniques, shelf stability, and most importantly scale-up for clinical trials are among the production obstacles.

Reference

1. Değim Z, Çelebi N, Alemdaroğlu C, Deveci M, Öztürk S, Özoğul C. Evaluation of chitosan gel containing liposome-loaded epidermal growth factor on burn wound healing. International Wound Journal. 2011 Aug;8(4):343-54.

2. Laurent A, Pantet O, Laurent L, Hirt-Burri N, De Buys Roessingh A, Raffoul W, Laurent P, Monod M, Applegate LA. Potency and stability of liposomal Amphotericin B formulated for topical management of Aspergillus spp. infections in burn patients. Burns Open. 2020; 4 (3): 110–6.

3. Blyth DM, Chung KK, Cancio LC, King BT, Murray CK. Clinical utility of fungal screening assays in adults with severe burns. Burns. 2013 May 1;39(3):413-9.

4. Jeschke MG, van Baar ME, Choudhry MA, Chung KK, Gibran NS, Logsetty S. Burn injury. Nature Reviews Disease Primers. 2020 Feb 13;6(1):11.

5. Hao D, Qu M, Nourbakhsh M. Experimental Study of Burn Damage Progression in a Human Composite Tissue Model. Biology 2021, 10, 40.

6. Abdul Rasool BK, Al Mahri N, Alburaimi N, Abdallah F, Shamma AS. A narrative review of the potential roles of lipid-based vesicles (vesiculosomes) in burn management. Scientia Pharmaceutica. 2022 Jun 29;90(3):39.

7. Pathak N, Pollard KJ. Lifestyle medicine prescriptions for personal and planetary health. The Journal of Climate Change and Health. 2021 Oct 1;4:100077.

8. Pathak M, Mhatre A. Clinical study to evaluate the efficacy of Madhutailika Basti in the management of Madhumehajanya Nadiprathan Shotha wrt Diabetic Neuropathy. Journal of Ayurveda and Integrated Medical Sciences. 2021 Feb 28;6(01):18-27.

9. Khan ZU, Ahmad S, Brazda A, Chandy R. Mucor circinelloides as a cause of invasive maxillofacial zygomycosis: an emerging dimorphic pathogen with reduced susceptibility to posaconazole. Journal of clinical microbiology. 2009 Apr;47(4):1244-

10. Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. Clinical microbiology reviews. 2006 Apr;19(2):403-34.

11. American Burn Association Consensus Conference on Burn Sepsis and Infection Group, Greenhalgh DG, Saffle JR, Holmes IV JH, Gamelli RL, Palmieri TL, Horton JW, Tompkins RG, Traber DL, Mozingo DW, Deitch EA. American Burn Association consensus conference to define sepsis and infection in burns. Journal of burn care & research. 2007 Nov 1;28(6):776-90.

12. Sharma BR. Infection in patients with severe burns: causes and prevention thereof. Infectious disease clinics of North America. 2007 Sep 1;21(3):745-59.

13. Neely AN, Brown RL, Clendening CE, Orloff MM, Gardner J, Greenhalgh DG. Proteolytic activity in human burn wounds. Wound Repair and Regeneration. 1997 Oct;5(4):302-9.

14. Joseph-Horne T, Hollomon DW. Molecular mechanisms of azole resistance in fungi. FEMS microbiology letters. 1997 Apr 1;149(2):141-9.

15. Joseph-Horne T, Hollomon DW. Molecular mechanisms of azole resistance in fungi. FEMS microbiology letters. 1997 Apr 1;149(2):141-9.

16. Samonte VA, Goto M, Ravindranath TM, Fazal N, Holloway VM, Goyal A, Gamelli RL, Sayeed MM. Exacerbation of intestinal permeability in rats after a two-hit injury: burn and Enterococcus faecalis infection. Critical care medicine. 2004 Nov1;32(11):2267-73.

17. Rasool BK, Hussain FN, Bahrainwala IM, Akbar N, Umar S, Kalady SP, Shamsheer Z. Advances in vaccine delivery strategies to promote effective immunization. Journal of Applied Pharmaceutical Science. 2022 May 5;12(5):001-26.

18. Agarwal S, Muniyandi P, Maekawa T, Kumar DS. Vesicular systems employing natural substances as promising drug candidates for MMP inhibition in glioblastoma: A nanotechnological approach. International Journal of Pharmaceutics. 2018 Nov 15;551(1-2):339-61.

19. Rommasi F, Esfandiari N. Liposomal nanomedicine: applications for drug delivery in cancer therapy. Nanoscale Research Letters. 2021 May 25;16(1):95.

20. Choudhury A, Sonowal K, Laskar RE, Deka D, Dey BK. Liposome: a carrier for effective drug delivery. Journal of Applied Pharmaceutical Research. 2020 Mar 30;8(1):228.

21. Sharma A, Sharma US. Liposomes in drug delivery: progress and limitations. International journal of pharmaceutics. 1997 Aug 26;154(2):123-40.

22. Babai I, Samira S, Barenholz Y, Zakay-Rones Z, Kedar E. A novel influenza subunit vaccine composed of liposome-encapsulated haemagglutinin/neuraminidase and IL-2or GM-CSF. I. Vaccine characterization and efficacy studies in mice. Vaccine. 1999 Mar 5;17(9-10):1223-38.

23. Banerjee R, Tyagi P, Li S, Huang L. Anisamide-targeted stealth liposomes: a potent carrier for targeting doxorubicin to human prostate cancer cells. International journal of cancer. 2004 Nov 20;112(4):693-700.

24. Li Z, Liu M, Wang H, Du S. Increased cutaneous wound healing effect of biodegradable liposomes containing madecassoside: Preparation optimization, *In vitro* dermal permeation, and in vivo bioevaluation. International journal of nanomedicine. 2016 Jun30:2995-3007.

25. Anwekar H, Patel S, Singhai AK. Liposome-as drug carriers. International journal of pharmacy & life sciences. 2011 Jul 1;2(7).

26. Johnson JR, Kuskowski MA, Wilt TJ. Systematic review: antimicrobial urinary catheters to prevent

catheter-associated urinary tract infection in hospitalized patients. Annals of Internal Medicine. 2006 Jan 17;144(2):116-26.

27. Pavelić Ž, Škalko-Basnet N, Filipović-Grčić J, Martinac A, Jalšenjak I. Development and *In vitro* evaluation of a liposomal vaginal delivery system for acyclovir. Journal of controlled release. 2005 Aug 18;106(1-2):34-43.

28. Hurler J, Engesland A, Poorahmary Kermany B, Škalko-Basnet N. Improved texture analysis for hydrogel characterization: Gel cohesiveness, adhesiveness, and hardness. Journal of Applied Polymer Science. 2012 Jul 5;125(1):180-8.

29. Hurler J, Žakelj S, Mravljak J, Pajk S, Kristl A, Schubert R, Škalko-Basnet N. The effect of lipid composition and liposome size on the release properties of liposomes-in- hydrogel. International journal of pharmaceutics. 2013 Nov 1;456(1):49-57.

30. Sheoran R, Khokra SL, Chawla V, Dureja H. Recent patents, formulation techniques, classification and characterization of liposomes. Recent patents on nanotechnology. 2019 Apr 1;13(1):17-27.

31. Perez AP, Altube MJ, Schilrreff P, Apezteguia G, Celes FS, Zacchino S, de Oliveira CI, Romero EL, Morilla MJ. Topical amphotericin B in ultra deformable liposomes: Formulation, skin penetration study, antifungal and antileishmanial activity *In vitro*. Colloids and Surfaces B: Biointerfaces. 2016 Mar 1;139:190-8.

32. Berkow EL, Lockhart SR, Ostrosky-Zeichner L. Antifungal susceptibility testing: current approaches. Clinical Microbiology Reviews. 2020 Jun 17;33(3):10-128.

33. Simpson IN, Gisby J, Hemingway CP, Durodie J, Macpherson I. Evaluation of mupirocin E-test for determination of isolate susceptibility: comparison with standard agar dilution techniques. Journal of clinical microbiology. 1995 Sep;33(9):2254-9.

34. Laurent A, Pantet O, Laurent L, Hirt-Burri N, de Buys Roessingh A, Raffoul W, Laurent P, Monod M, Applegate LA. Potency and stability of liposomal Amphotericin B formulated for topical management of Aspergillus spp. infections in burn patients. Burns Open. 2020 Jul 1;4(3):110-6. 34.

35. Jones DS, Woolfson AD, Brown AF, Coulter WA, McClelland C, Irwin CR. Design, characterization, and preliminary clinical evaluation of a novel mucoadhesive topical formulation containing tetracycline for the treatment of periodontal disease. Journal ofControlled Release. 2000 Jul 3;67(2-3):357-68.

36. Sˇ kalko NA, Cˇ ajkovac M, Jalsˇ enjak I. Liposomes with metronidazole for topical use: the choice of preparation method and vehicle. Journal of liposome research. 1998Jan 1;8(2):283-93. 36.

37. Ehrlich P. Collected studies on immunity. J. Wiley & sons; 1910.

38. Değim Z, Çelebi N, Alemdaroğlu C, Deveci M, Öztürk S, Özoğul C. Evaluation of chitosan gel containing liposome-loaded epidermal growth factor on burn wound healing. International Wound Journal. 2011 Aug;8(4):343-54.

39. Kalepu S, Sunilkumar KT, Betha S, Mohanvarma M. Liposomal drug delivery system—a comprehensive review. Int J Drug Dev Res. 2013 Oct;5(4):62-75.

40. Samad A, Sultana Y, Aqil M. Liposomal drug delivery systems: an updated review. Current drug delivery. 2007 Oct 1;4(4):297-305.

41. Ogundipe KO, Adigun IA, Solagberu BA. Economic burden of drug use in patients with acute burns: experience in a developing country. Journal of Tropical Medicine. 2009 Aug 31;2009.

42. Leppert W, Malec–Milewska M, Zajaczkowska R, Wordliczek J. Transdermal and topical drug administration in the treatment of pain. Molecules. 2018 Mar 17;23(3):681.

43. Norman G, Christie J, Liu Z, Westby MJ, Jefferies JM, Hudson T, Edwards J, Mohapatra DP, Hassan IA, Dumville JC. Antiseptics for burns. Cochrane Database of Systematic Reviews. 2017(7).

44. Cancio LC. Topical antimicrobial agents for burn wound care: history and current status. Surgical Infections. 2021 Feb 1;22(1):3-11.

45. Gowda BH, Mohanto S, Singh A, Bhunia A, Abdelgawad MA, Ghosh S, Ansari MJ, Pramanik S. Nanoparticle-based therapeutic approaches for wound healing: a review of the state-of-the-art. Materials Today Chemistry. 2023 Jan 1;27:101319.

46. Pruskowski KA, Mitchell TA, Kiley JL, Wellington T, Britton GW, Cancio LC. Diagnosis and Management of Invasive Fungal Wound Infections in Burn Patients. European Burn Journal. 2021 Oct 1;2(4):168-83.

47. Altoparlak U, Erol S, Akcay MN, Celebi F, Kadanali A. The time-related changes of antimicrobial resistance patterns and predominant bacterial profiles of burn wounds and body flora of burned patients. Burns. 2004 Nov 1;30(7):660-4.

48. Elliott TS, Lambert PA. Antibacterial resistance in the intensive care unit: mechanisms and management. British medical bulletin. 1999 Jan 1;55(1):259-76.

49. Afshari A, Nguyen L, Kahn SA, Montgomery AC, Shinha T, Stratton C, Summitt B. The effective duration of antimicrobial activity of Mafenide acetate after reconstitution. Journal of Burn Care & Research. 2018 Aug 17;39(5):736-8.

50. Gallagher JJ, Williams-Bouyer N, Villarreal C, Heggers JP, Herndon DN. Treatment of infection in burns. Total Burn Care. Philadelphia: Elsevier, Inc. 2007 Jan 1:136-76.

51. Heggers JP, Robson MC, Herndon DN, Desai MH. The efficacy of nystatin combined with topical microbial agents in the treatment of burn wound sepsis. The Journal of Burn Care & Rehabilitation. 1989 Nov 1;10(6):508-11.

52. Monafo WW, West MA. Current treatment recommendations for topical burn therapy. Drugs. 1990 Sep;40:364-73.

53. Johnson BA, Anker H, Meleney FL. Bacitracin: a new antibiotic produced by a member of the B. subtilis group. Science. 1945 Oct 12;102(2650):376-7.

54. Alvarez OM, inventor; Bioderm Inc, assignee. Zinc bacitracin containing wound dressing. United States patent US 5,061,689. 1991 Oct 29.

55. Palmieri TL, Greenhalgh DG. Topical treatment of pediatric patients with burns: a practical guide. American journal of clinical dermatology. 2002 Dec;3:529-34.

56. Rode H, Hanslo D, De Wet PM, Millar AJ, Cywes S. Efficacy of mupirocin in methicillin-resistant Staphylococcus aureus burn wound infection. Antimicrobial agents and chemotherapy. 1989 Aug;33(8):1358-61.

57. Strock LL, Lee MM, Rutan RL, Desai MH, Robson MC, Herndon DN, Heggers JP. Topical Bactroban (Mupirocin) efficacy in treating burn wounds infected with methicillin-resistant staphylococci. The Journal of burn care & rehabilitation. 1990 Sep1;11(5):454-9.

58. Drogemoller ML, Linley SL, inventors; SmithKline Beecham Pharmaceuticals Pty Ltd, assignee. Composition comprising mupirocin and chlorhexidine. United States patent US 6,214,866. 2001 Apr 10.

59. Donskey CJ. Does improving surface cleaning and disinfection reduce healthcare- associated infections? American journal of infection control. 2013 May 1;41(5):S12-9.

60. Meier PA, Carter CD, Wallace SE, Hollis RJ, Pfaller MA, Herwaldt LA. A prolonged outbreak of methicillin-resistant Staphylococcus aureus in the burn unit of a tertiary medical center. Infection Control & Hospital Epidemiology. 1996 Dec;17(12):798-802.

61. Sinha R, Agarwal RK, Agarwal M. Povidone iodine plus neosporin in superficial burns—a continuing study. Burns. 1997 Nov 1;23(7-8):626-8.

62. Munster AM. Treatment of invasive Enterobacter cloacae burns wound sepsis with topical nitrofurazone. The Journal of Trauma. 1984 Jun 1;24(6):524-5.

63. Darouiche RO, Raad II, Heard SO, Thornby JI, Wenker OC, Gabrielli A, Berg J, Khardori N, Hanna H, Hachem R, Harris RL. A comparison of two antimicrobial- impregnated central venous catheters. New England Journal of Medicine. 1999 Jan 7;340(1):1-8.

64. Guay DR. An update on the role of nitrofurans in the management of urinary tract infections. Drugs. 2001 Mar;61:353-64.

65. Fox Jr CL, Modak SM. Mechanism of silver sulfadiazine action on burn wound infections. Antimicrobial agents and chemotherapy. 1974 Jun;5(6):582-8.

66. Atiyeh BS, Costagliola M, Hayek SN, Dibo SA. Effect of silver on burn wound infection control and healing: a review of the literature. burns. 2007 Mar 1;33(2):139- 48.

67. Klasen HJ. A historical review of the use of silver in the treatment of burns. II. Renewed interest in silver. Burns. 2000 Mar 1;26(2):131-8.

68. Lee AR, Leem H, Lee J, Park KC. Reversal of silver sulfadiazine-impaired wound healing by epidermal growth factor. Biomaterials. 2005 Aug 1;26(22):4670-6.

69. Rosenkranz HS, Coward JE, Wlodkowski TJ, Carr HS. Properties of silver sulfadiazine-resistant Enterobacter cloacae. Antimicrobial agents and chemotherapy. 1974 Feb;5(2):199-201.

70. Modak SH, Fox Jr CL. Synergistic action of silver sulfadiazine and sodium piperacillin on resistant Pseudomonas aeruginosa *In vitro* and experimental burn wound infections. The Journal of Trauma. 1985 Jan 1;25(1):27-31.

71. Chen JR, inventor; Sage Pharmaceuticals Inc, assignee. Topical spray for burn treatment and antiinfection. United States patent US 6,987,133. 2006 Jan 17.

72. Fox C, inventor; Research Corp, assignee. Silver sulfadiazine is used in the treatment of burns. United States patent US 3,761,590. 1973 Sep 25.

73. Fox Jr CL, Modak SM, Fox P, inventors; Genetic Laboratories Inc, assignee. A wound dressing comprising

silver sulfadiazine incorporated in animal tissue and method of preparation. United States patent US 4,599,226. 1986 July 8.

74. Price CI, Horton JW, Baxter CR. Topical liposomal delivery of antibiotics in soft tissue infection. Journal of Surgical Research. 1990 Aug 1;49(2):174-8.

75. Laurent A, Pantet O, Laurent L, Hirt-Burri N, de Buys Roessingh A, Raffoul W, Laurent P, Monod M, Applegate LA. Potency and stability of liposomal Amphotericin B formulated for topical management of Aspergillus spp. infections in burn patients. Burns Open. 2020 Jul 1;4(3):110-6.

76. Ferreira M, Ogren M, Dias JN, Silva M, Gil S, Tavares L, Aires-da-Silva F, Gaspar MM, Aguiar SI. Liposomes as antibiotic delivery systems: A promising nanotechnological strategy against antimicrobial resistance. Molecules. 2021 Apr 2;26(7):2047.

77. Hamedi H, Moradi S, Hudson SM, Tonelli AE. Chitosan-based hydrogels and their applications for drug delivery in wound dressings: A review. Carbohydrate polymers. 2018 Nov 1;199:445-60. 77.

78. Boyd AN, Blair ME, Degenkolb KE, Foster DR, Hartman BC, Sood R, Walroth TA. A prospective analysis describing the innovative use of liposomal bupivacaine in burn patients. Burns. 2020 Mar 1;46(2):370-6.

79. Filipczak N, Pan J, Yalamarty SS, Torchilin VP. Recent advancements in liposome technology. Advanced drug delivery reviews. 2020 Jan 1;156:4-22.

80. Bell A, Hart J. Evaluation of two absorbent silver dressings in a porcine partial- thickness excisional wound model. Journal of wound care. 2007 Oct;16(10):445-53.

81. Thomas S, McCubbin P. An *In vitro* analysis of the antimicrobial properties of 10 silver-containing dressings. Journal of wound care. 2003 Sep;12(8):305-8.

82. Khalili A, Alipour S, Fathalipour M, Purkhosrow A, Bayat G, Nekooeian AA. Liposomal and non-liposomal formulations of vitamin C: Comparison of the antihypertensive and vascular modifying activity in renovascular hypertensive rats. Iranian Journal of Medical Sciences. 2020 Jan;45(1):41.Reolon JB, Sari MH, Marchiori C, Dallabrida KG, dos Santos JA, de Almeida ID, Alves FM, Bonini JS, Ferreira LM. Herbal drugs-loaded soft nanoparticles for treating skin disorders: Where do we stand? Industrial Crops and Products. 2023 Dec 15;206:117602.

83. Lee JE, Park JC, Lee KH, Oh SH, Suh H. Laminin Modified Infection-Preventing Collagen Membrane Containing Silver Sulfadiazine–Hyaluronan Microparticles. Artificial organs. 2002 Jun;26(6):521-8.

84. Sari MH, Cobre AD, Pontarolo R, Ferreira LM. Status and Future Scope of Soft Nanoparticles-Based Hydrogel in Wound Healing. Pharmaceutics. 2023 Mar 8;15(3):874.

85. Haberal M, Oner Z, Bayraktar U, Bilgin N. The use of silver nitrate-incorporated amniotic membrane as a temporary dressing. Burns. 1987 Apr 1;13(2):159-63.

86. Patel PM, inventor; Ferndale IP Inc, assignee. High-concentration lidocaine compositions and methods for their preparation. United States patent US 7,476,400. 2009 Jan 13.

87. Santana Millán H, Ventosa N, Martínez Díaz E, Berlanga Acosta J, Cabrera I, Veciana J. Vesicules which include epidermal growth factor and compositions that contain same.

88. Huang AL, Wu G, inventors; LiveLeaf Inc, assignee. Enhanced antivirulent for antibiotic-resistant

bacteria. United States patent application US 16/589,955. 2020 Sep3.

89. Azevedo MM, Pina-Vaz C, Rodrigues AG. The role of phage therapy in burn wound infections management: advantages and pitfalls. Journal of Burn Care & Research. 2022 Mar 1;43(2):336-42. 90. Rigby KL. Novel Microbe-Resistant Clay Dressing for Healing Burn Wounds.

90. Khan AD, Rastogi V, LAVHALE P, Jain J. Novel Approaches for Herbal Drug Delivery in Wound.