July - October 2019; 8(4): 1-12

International Journal of Research and Development in Pharmacy & Life Science
International open access peer-reviewed journal
ISSN (P): 2393-932X, ISSN (E): 2278-0238
Journal homepage: http://ijrdpl.com

Review Article

An overview of Novel Drug Delivery Systems for Acne

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Keywords: Acne, Antibiotics, Drug Delivery System, Liposomes, Microsphere, Oral contraceptives

Article Information:

Received: May 31, 2019;
Revised: June 21, 2019;
Accepted: July 01, 2019
Available online on:
15.10.2019@http://ijrdpl.com

http://dx.doi.org/10.21276/IJRDPL.2278-0238.2019.8(4).1-12

ABSTRACT: *Acne vulgaris* is a type of chronic disease of the skin which is mainly caused by the blockage in the sebaceous gland or having any inflammation in those glands which is together is known as pilosebaceous units. It mainly affects the areas having the highest number of sebaceous follicles; those are the face, the back and upper region of the chest. It is a disease that mainly affects the adolescent age group but can be found in any age group. These are present as inflammatory pustules, papules, cysts and nodules, non-inflammatory closed comedones (whiteheads), ripen comedones (blackheads), or a mixture of lesions. Acne is most commonly seen in almost every human being at some point in their lives. There are 20-25 chances of progression of acne to the severe case which leads to permanent scarring. These complications lead to psychological problems like depression, social isolation, lowered self-esteem, and lowered self-confidence. The aim of treating acne is to prevent severe and long-term complications. The present review focuses on novel drug delivery systems for the treatment of acne. It also includes conventional treatments currently available in the market, its limitation and different strategies to overcome these limitations.

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INTRODUCTION

Approximately 95% of the total population faces the problem of Acne in their lives for at least once. The Acne can be of any type either pustules, cysts, comedones, papules, and scarring can also be seen. Acne responds to hormones also either it is endogenous or exogenous. It is a chronic inflammatory disorder of the pilosebaceous units on the face and other regions comprising of the follicular canal and the bunch of sebaceous glands that surround the follicle.

Pathophysiology of Acne consists of differentiation in keratinocytes, hyperproliferation of *Propionibacterium acne*, increased sebum production, and inflammatory response initiated by any foreign material like antigens or cytokine, etc. Comedones on the face are formed by overproduction of androsterone and oil-producing glands in the face. The primary 2 types of non-inflammatory comedones are 1) The closed comedones (whitehead) and 2) The ripen/open comedones (blackhead).

The main target of using Novel drug delivery system to the skin through topical agents is to minimize the risk of the irritant property of some anti-acne medicaments and also shows the great efficiency through it.

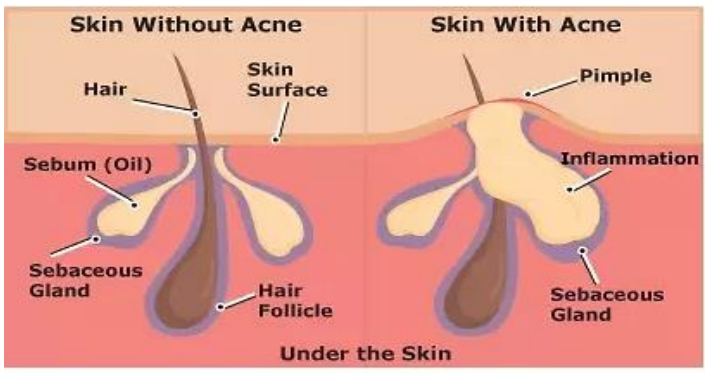

Fig. 1: Difference between regular skin and skin affected with acne (http://skinspecialistinrajendranagar.com/what-causes-acne-whats-the-difference-in-a-normal-skin-and-a-skin-with-acne/)

DIFFERENT TYPES OF ACNE

Minor acne can be cured at home or by using any over-the-counter (OTC) medicines. However, if the acne tends to go in severe cases or any long-term skin inflammation it should immediately get treated by any specialist or dermatologist. About 85% of teenagers and young adults deal with it. The commonly known types of acne are;

1) Whiteheads
2) Blackheads
3) Pustules, or commonly known as pimple
4) Nodules
5) Cysts
6) Papules

1. Non-inflammatory acne types

Whiteheads and Blackheads are two categories of non-inflammatory acne. They are not very painful and do not cause any kind of swelling. They have less severe than others.

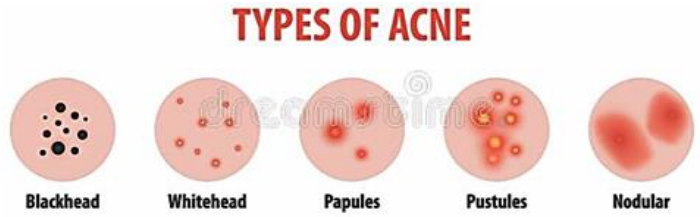

Fig. 2: Different types of Acne

http://www.thereviveblog.com/types-of-acne-and-how-to-treat-them

1. Whiteheads

They are known as closed comedones in medical terms. They are small white, flesh-colored spots. The structure of the whitehead is somewhat like a white center around a red hole. Sometimes the hair emerges from the white center but in most cases, the hair can be seen trapped in the center. The skin around the whitehead gets tight or wrinkled especially when the whiteheads are big or are raised. They do not cause scarring.

2. Blackheads

They are known as ripening or open comedones. They are usually black or dark-colored spots that appear slightly raised. The skin surrounding the blackheads appears to be normal and blackheads are darker than its surroundings.

Treatment Option

One can use over-the-counter formulations available in the market in the form of gels, rinses, creams, toners, and moisturizers to treat comedones. Many ayurvedic and home remedies can also be used to treat them. Some basic daily routine can also help in minimizing and treating the comedones those are as follows;

- Wash the face with lukewarm water and soap 2 times a day.
- Reducing stress
- Eating a healthy and balanced diet.

3. Inflammatory Acne type

Inflammatory acne is:

a) Papules
b) Pustules
c) Cysts
d) Nodules

Minor to a mild form

- **Papules-** these are bumps present under the skin surface. They are solid, pink, tender, and raised. The skin around it mostly red or pinkish and is swollen.
- **Pustules** (pimples)- they look like an elongated whitehead which is inflamed.

Moderate to severe form

- **Nodules-** they are hard, inflamed, painful lump which is located deep with the skin. They are the severe form of acne and they can cause various skin problems like scarring and dark spots.
- **Cysts-** they are situated deep within the skin and generally the hard, painful and their color may be red or sometimes white. They are filled with pus. They are formed deeper within the skin even deeper than the nodules. They are the most severe case of acne and they also cause permanent skin complications.

Treatment options

a) Drainage and extraction to remove large cysts.
b) Use of steroidal injections
c) Use of topical corticosteroids

Mechanism and causes of acne

Pathogenesis

1. Occlusion of the pilosebaceous orifice
2. Increased sebum secretion
3. Microbial colonization
4. Release of inflammatory mediator

Epidemiology

Prevalence- affects most of the adolescent.

Age- between 12- 14 years.

Gender- in this both the sexes are equally affected but the nodulocystic type of acne is most common in males.

Morphology

Polymorphic eruption of all types of acne on the background of oiliness.

Causes

There are four major causes for any type of acne to occur those are as follows:

a) Excess oil production and retention of oil on the skin for a long time.
b) Hair follicles clogged by skin dead cells along with the presence of oils.
c) Bacteria
d) Excess secretion and activity of male hormone i.e. androgens.

STATUS OF ACNE

The seriousness of acne is measured according to the collective acne intensity classification. This categorized them into mild, moderate, and severe based on count and types of acne. According to research and surveys, the global market for acne was worth $2800 million in 2009. Also, it was estimated to reach $3020 million by 2016. The present market contains many different types of products that target acne through different factors even in the development of acne. In India, according to a report generated in 2009, the market of anti-acne products was 1.3 billion and is growing by the rate of 14% each year.

TREATMENT STRATEGIES USED FOR ACNE

The treatment option in this varies with the phase and degree of disease. No simple treatment can be given. To treat the mild and moderate form of acne the topical method is always the first choice and systemic treatment is given if the disease becomes severe or moderate. Treatment of acne is done by the following three ways:

a) Topical treatment- it only contains the usage of antibiotics, retinoids, or a combination of both medicaments. Topical medications are exasperating to the skin.
b) Systemic treatment- it contains oral antibiotics retinoids and hormonal treatment. This is given the case of severe or moderate acne types or when there is a resistant towards the topical treatment or if the acne is present in the area of the body.
c) Treatments are other than those which were not mentioned anywhere above. Two categories like resurfacing, chemical peels, xenografts, heterografts, and fat transplant.

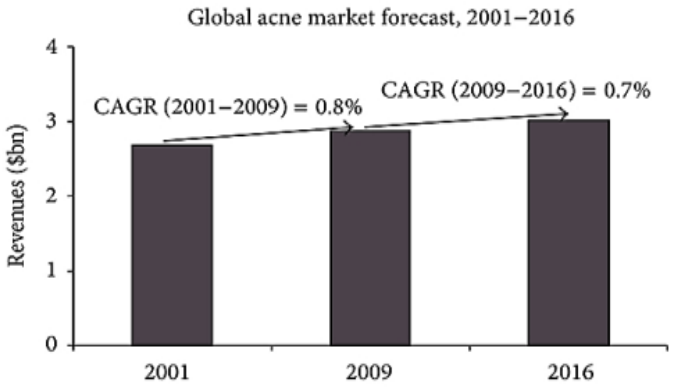

Fig. 3: Future Forecast of Acne (https://www.researchgate.net/figure/Futureforecast-of-acne_fig2_261257504)

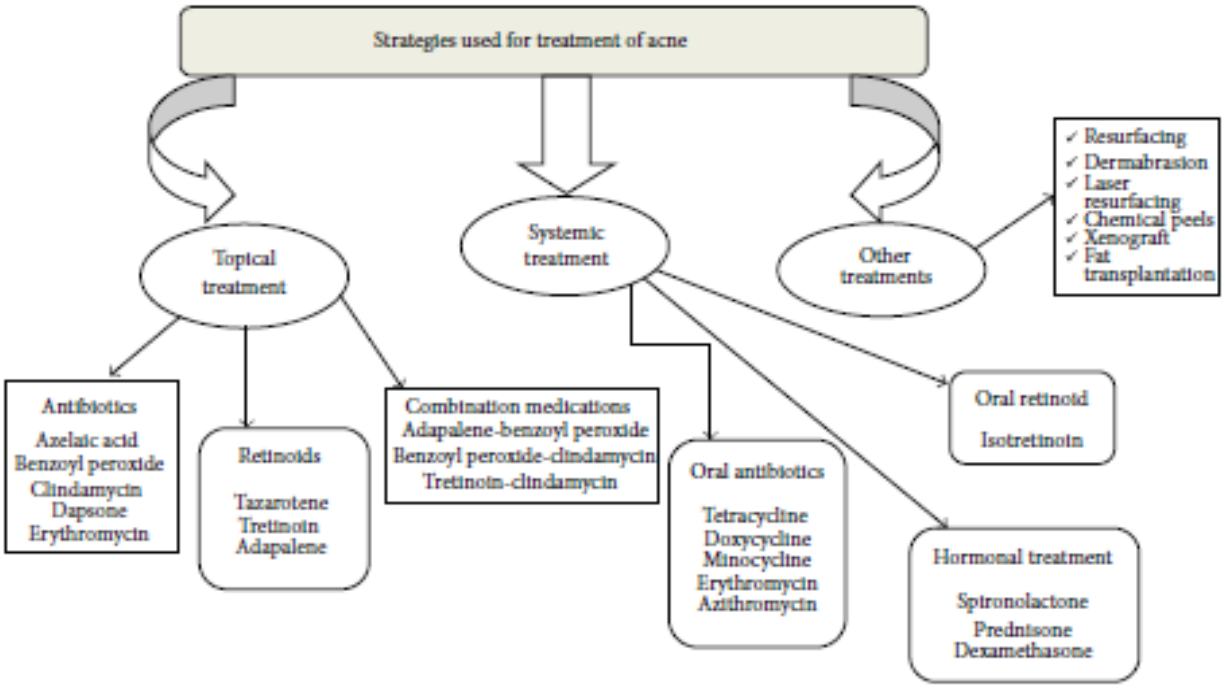

Fig. 4: Strategies to treat Acne (https://www.researchgate.net/figure/Treatment-strategies-used-for-acne_fig4_261257504**)**

Table 1: Different type of Acne concerning their severity

S. No.	Type of acne	Features
1	Mild acne	Less than 20 comedones or less than 15 inflammatory lesions, or total lesion count lesser than 30
2	Moderate acne	20 to 100 comedones, or 10 to 50 inflammatory lesions, or a total of 30 to 125
3	Severe acne	More than 5 nodules, and if the total inflammatory count is greater than 50, or total lesion count is greater than 125

Table 2: Different types of Acne

S. No.	Types of Acne	Features	Reference
1	Comedones (non-inflammatory)	*Whitehead (closed):* it is an obstructed skin opening that contains a hair follicle with sebum, keratin, and the bacteria. *Blackhead (open):* it is a wide opening to the skin covered with the black mass of dead skin debris and contains a hair follicle with sebum, keratin, and bacteria.	[50]
2	Papulopustular (inflammatory)	*Papule:* small bump smaller than 5 mm in diameter. *Pustule:* smaller bump with a visible central core of purulent material.	[50]
3	Nodular (inflammatory)	*Nodule:* the size of the bump is greater than 5 mm in diameter	[50]

Table 3: Different types of antibiotics

Antibiotic	Name	Dose	Duration	Drawbacks	Reference
Antibiotics (oral)	Tetracycline, Oxytetracycline	250 to 500mg two times a day	4 to 6 months	The gastro-intestinal problem, vaginal candidiasis, development of resistance	[1]
Tetracyclines	Minocycline	50 to 100 mg two times a day	4 to 6 months	Vertigo, hyperpigmentation of skin and oral mucosa, the cost is high	[1]

Table 4: Treatment using Hormones

Name	Dose	Duration	Drawbacks	Reference
Spironolactone	25 to 100 mg two times a day	24 weeks	Menstrual irregularities, contraindication in pregnancy	[1]
Prednisone	2.5 to 5mg daily	Indefinitely	loss of appetite, heartburn, trouble sleeping	[1]
Dexamethasone	0.125 to 0.5mg daily	Indefinitely	Adrenal suppression	[1]
Cryprotene acetate/ethinyl Estradiol (oral contraceptives)	2mg/30 to 50µg	24 weeks	Vascular thrombosis, melasma, weight gain	[1]
Levonorgestrel/ethinylestradiol	100 µg/20 µg	24 weeks	Vascular thrombosis, melasma, weight gain	[1]

CONVENTIONAL DELIVERY SYSTEM USED IN THE TREATMENT OF ACNE

In the early days, a conventional delivery system was used for treating acne. In around 1950, the use of antibiotics was increased as they were more effective because of the anti-inflammatory effect of tetracycline. In 1980, Accutane a type of vitamin A was made for reducing the oils in the skin and skin glands. In 1990 laser treatment was adopted to treat acne and later on it was observed that the use of laser technology is effective for the nodular and cystic type of acne. The conventional delivery system shows effect by using any of the four mechanisms namely; normalizing shedding into the pore to prevent blockage, killing bacteria responsible for acne, anti-inflammatory therapy, and hormonal treatment. Many patients fail to respond towards the treatment of acne despite having so many treatments or develop side effect that affects the patients and hinders the compliance and compromising the efficiency of therapy in patients. To reduce the risk of the above-mentioned side effects the development of novel drug delivery came to existence. They decrease the irritant property of the moiety without altering the efficacy. The novel delivery system penetrates right into the skin more efficiently and goes straight towards the hair follicles.

NOVEL DRUG DELIVERY SYSTEM USED TO TREAT ACNE

The use of the novel delivery system provides a better efficacy of the antiacne topical agents, but the adverse effects like irritation, redness, peeling, dryness, and scaling still are the major issues. The novel delivery systems are specially prepared to amplify the load ability of active ingredients and decrease the side effects of it. The novel delivery systems which are under development for use topically in treating acne include liposomes, niosomes, microsponge, microemulsions, microsphere, hydrogel, aerosol, and so forth. The mechanisms of drug release in the novel carrier system are basically of two types: diffusion through the carrier matrix and erosion. Sometimes a combination of erosion and diffusion method is also present. As the novel carrier system is advantageous but it also carries some serious drawbacks which limit their usage. Drugs passively can lead to low drug loading efficacy, any error during preparation and preservation, and leakage.

Table 5: Side effects associated with the conventional formulations used.

Conventional delivery system	Drug	Side Effects	Reference
Lotion	Benzoyl peroxide	Peeling, itching, redness, drying,	[51]
	Clindamycin	Peeling, redness, dryness	[52]
	Tretinoin	Peeling, itching, redness.	[53]
	Erythromycin	Erythema, scaling, burning.	[54]
	Glycolic acid	Erythema, scaling, burning.	[55]
Cream	Adapalene	Erythema, scaling, dryness.	[56]
	Tazarotene	Erythema, scaling, burning.	[57]
	Azelaic acid	Itching, rash, pruritus.	[55]
	Tea oil	Burning, itching, irritation.	[58]
	Clindamycin	Erythema, desquamation	[59]
Gel	Salicylic acid	Erythema, dryness, dermatitis.	[51; 60]
	Erythromycin	Dryness, erythema, peeling.	[54; 61]
	Benzoyl peroxide	Dryness, erythema, peeling, dermatitis.	[61]
	Dapsone	Erythema, scaling, dryness.	[62]
Emollient	Sodium sulfacetamide sulfur	Dryness, irritation, redness, scaling, stinging, burning.	[63]

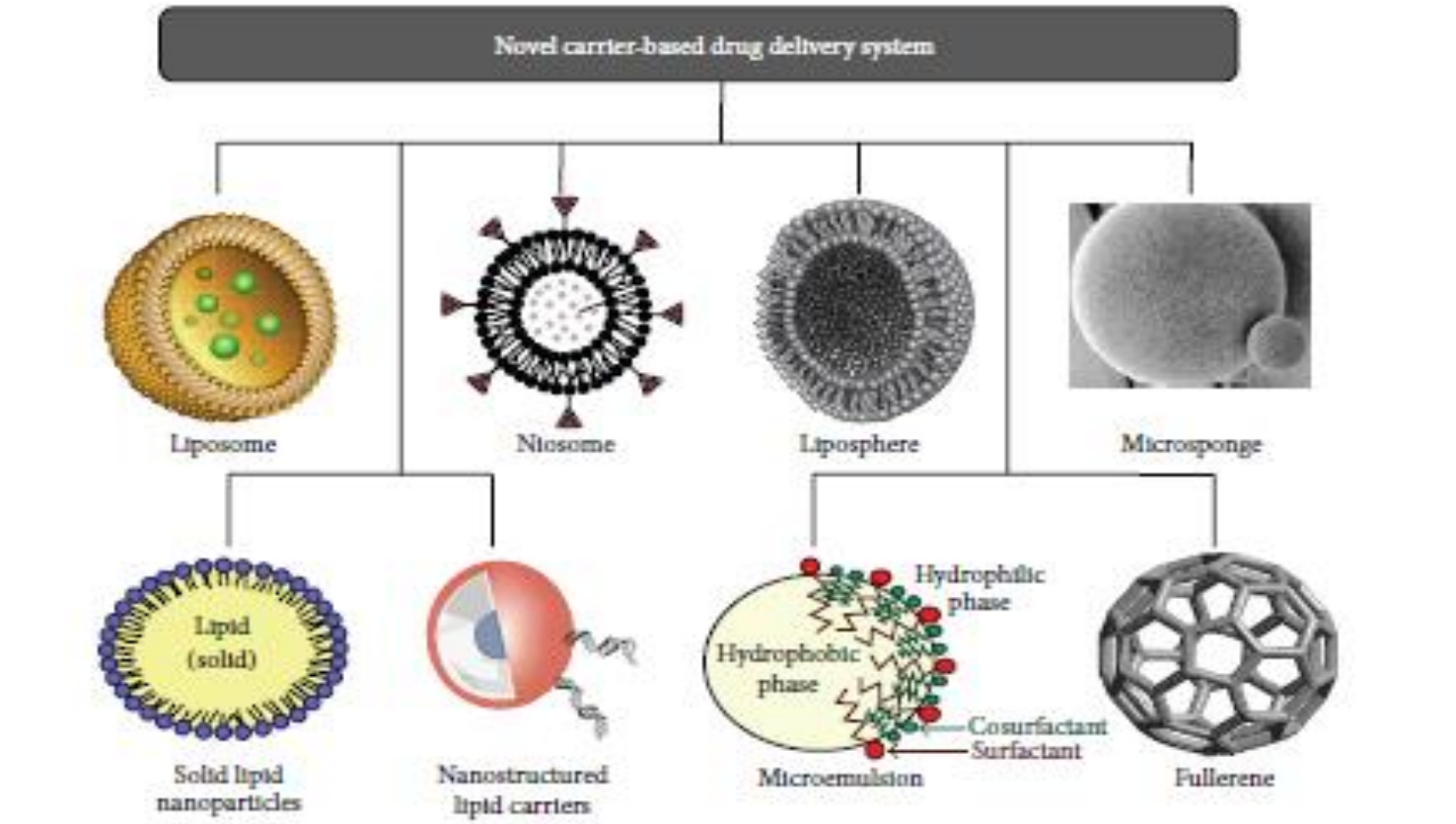

Fig. 5: Novel carrier-based drug delivery system for treatment of Acne (https://www.researchgate.net/figure/Novel-carrier-based-drug-delivery-system-for-treatment-of-acne_fig1_261257504)

1) Liposomes

They are concentric bilayered vesicles in which there is an aqueous core that is enclosed in a membranous lipid bilayer mostly of natural or synthetic phospholipids. They are mainly used for treating diseases associated with hair follicles like Acne. They are artificial vesicle which is spherical and they are made up from the non-toxic phospholipids. They are a promising system for drug delivery because of their size, hydrophobic and hydrophilic properties [28-30]. Their properties vary considerably with the difference in lipid composition, charge on the surface, size, or the process used for preparing the liposomes. Rigidity and fluid nature and the charge of the bilayer are solely depending on the components of the bilayers. For example; unsaturated phosphatidylcholine type from natural sources like eggs or soybean, they provide much permeable and a lesser stable bilayer, whereas saturated phospholipids having longer acyl chain, forms a rigid, or rather an impermeable structure [28-30]. Due to their promising properties like biocompatibility, biodegradability, lowered toxicity and tendency to trap both hydrophilic and hydrophobic drug molecules [31] and simplify the delivery of site-specified drugs to tumor tissues they have both amplified rate in investigational system and commercially as drug delivery system [17,32].

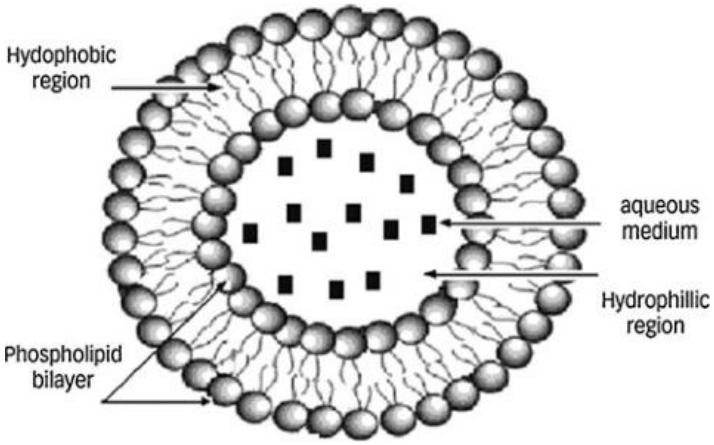

Fig. 6: Structure of Liposome

https://www.researchgate.net/figure/Liposome-structure-where-the-coating-or-outer-membrane-consists-of-one-or-more-hydrated_fig3_236119384

Advantage of Liposomes

When used topically, they can increase the deposition of the drug at the site of action within the skin, absorption in the systemic circulation is reduced that minimizes the adverse effect thereby provides local effect and the direct target the skin appendages. The vesicular system leads to good results in treating the acne as a comparison to a conventional system by the release of the drug on target present in the skin and are more preferable for the lipophilic drug.

Disadvantages of Liposomes

The major demerit of this preparation type is its stability. Stability issues arise from several problems; formation of the ice crystals in the liposomes and instability in bilayers which leads to leakage of the enclosed material. Other reasons are oxidation of cholesterol and phospholipids which results in formulation instability. Hydrolysis and oxidation of lipids show the chemical instability. Destabilization is due to the exchange between the liposome and HDLs.

2) Niosomes

They are the unilamellar or multilamellar vesicles in which there is an aqueous core surrounded by bilayer made up of non-ionic surfactants. They are non-ionic surfactant vesicles because of which the skin penetration is increased in the skin. They are said to be the best carriers among the others [20]. The difference in the composition of the vesicle, lamellarity, surface charge, size, and concentration change the properties of the vesicle. The niosomes can accommodate drugs with an enormous range of solubility because of the presence of hydrophilic, amphiphilic, and lipophilic parts in the structure [21]. The therapeutic property of drugs can also be amplified by delayed clearance from the circulatory system that protects the drug from the environment and restricts the effects of affected cells [22]. The ideals properties of the surfactants that are used in the noisome formulation should be biocompatible, biodegradable, and non-immunogenic [26]. They are used to study the reaction of the immune system provoked by antigens [23]. They are also used as a carrier for hemoglobin [24,25]. The niosomal vesicular system provides better drug concentration by oral, parenteral, or topical routes at the site of action. The progress in the niosomal drug delivery system is still in the primitive stages, but it has shown a promising property in cancer chemotherapy and anti-leishmanial therapy [27,18].

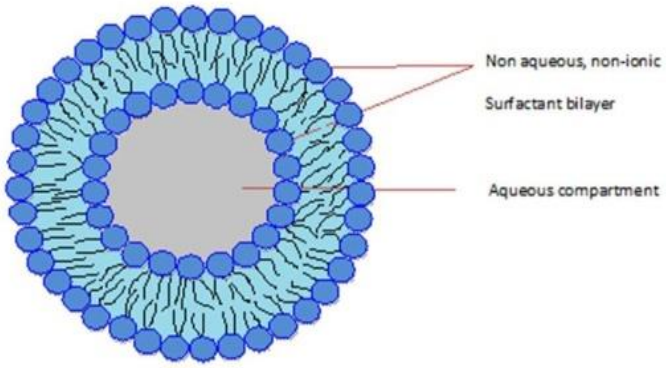

Fig. 7: Structure of Niosomes
https://www.researchgate.net/figure/Structure-of-niosomes-Characteristic-features-of-Niosomes-i-Niosomes-are-highly_fig1_327281294

Advantages of Niosomes

The systemic absorption of the drug can be reduced and the residence time of the drug in the epidermis and stratum corneum can be increased by using a niosomal preparation topically. Niosomes are used over liposomes because of the former exhibit high stability chemically and economy. The reason for the preparation of niosomes is that they have the higher chemical stability of the surfactants than that of phospholipids due to ester bond, phospholipids can be easily hydrolyzed.

Disadvantages of Niosomes

As niosomes are superior to liposomes, they still have some stability problems with them like physical stability of fusion, aggregation, sedimentation, and leakage on storage. The major issue is the hydrolysis of encapsulated drugs which alters the shelf life of the dispersion in niosomes.

3) Microsponges

They are the patented polymeric drug delivery system that contains porous microspheres in which an enormous range of actives such as essential oils, anti-fungal, anti-inflammatory agents are easily enclosed. They have a true nature of a sponge that contains a myriad of interconnecting voids. Their size range varies from 5 – 300 µm in diameter that depends upon the intensity of after-feel required or smoothness needed for the end formula. They may vary in sizes but a typical 25 µm sphere has almost several pores up to 250000. The microsponges contain a huge reservoir within each of them that can be loaded up to its weight of the active agent. The porous nature of microsponges adds to its safety as it can entrap the bacterial contamination. Because of the smaller pore size, the bacteria ranging from 0.007 to 0.2 µm cannot penetrate the structure of microsponges [19,33].

Advantage of Microsponges

In this, the release of the drug can be controlled by diffusion or other parameters like pH, moisture, and friction, or skin temperature. They are also capable of enhancing the absorption of secretions of the skin, therefore, reducing the oiliness. These polymers tend to load a wide variety of APIs which provides the benefits of amplified efficacy along with mildness and tolerability. This system has ranged over pH 1-11 and temperature up to 130 Celsius and is compatible with most of the vehicles and ingredients, self-sterilizing average pore size is 0.25µm.

4) Microemulsions

They are transparent dispersion of oil in water with the size of droplet about 100nm in diameter. They are stabilized with the film of surfactant and co-surfactant. They are thermodynamically stable, clear, and optically isotropic systems. They are prepared by step-wise mixing of suitable oil, water, and an amphiphile [35-38]. They were used to solubilize drugs and to enhance the availability of the drug [39]. It has said that they can dissolve the structure of lipids present in the stratum corneum which leads to the loss barrier properties of the skin [34,40].

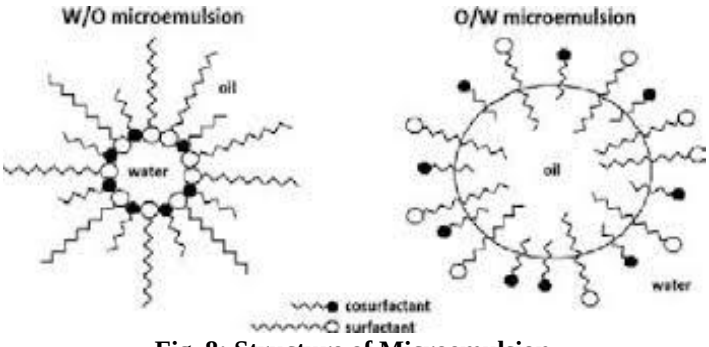

Fig. 8: Structure of Microemulsion

https://www.researchgate.net/figure/Schematic-representation-of-w-o-microemulsion-and-o-w-microemulsion-structure_fig2_49843495

5) Nanoemulsion

They are a colloidal particulate system that is in the range of sub-micron size which acts as a carrier of the drug moiety. The size range varies from 10 to 1000 nm. They are negatively charged amorphous and lipophilic surfaces and are solid spheres. They are used as a drug delivery system because they have amplified therapeutic efficiency regarding the drug and minimize the side effects and toxic reactions in the body [41].

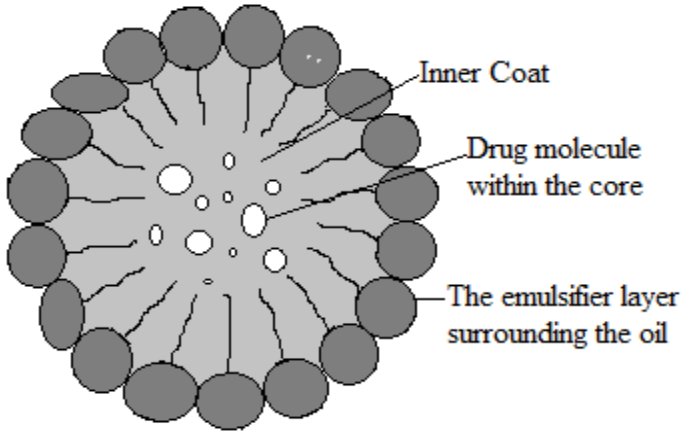

Fig. 9: Structure of Nanoemulsion

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6) Microsphere

They are made up of biodegradable polymer and are spherical. It is filled with the drug substances and is dispersed and when it gets degraded to release the drug. The microencapsulation technique is used to prepare the microspheres. They can be prepared in a definite size and shape which by default improves delivery of the drug to the specified site. Porous microspheres are fabricated with either internal or external porosity, or even a combination of both, with or without interconnectivity for cell attachment. The Microspheres can be assembled into 3-Dimensional porous scaffolds or as a stand-alone product [42].

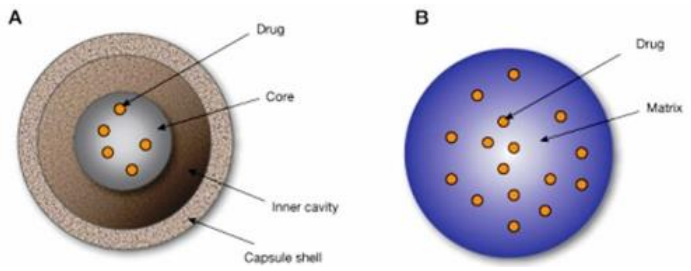

Fig. 10: Structure of Microsphere

https://www.intmedpress.com/journals/avcc/popup_fig.cfm?img=d56deee6-7da1-4d96-8b71-697b356f2553

Advantages of Microsphere

When administered in skin the free drug present in the preparation penetrates the epidermis layer and compensates by the release of drugs from the microsphere. The formulation of topical tretinoin and benzoyl peroxide has proven good efficiency and tolerability and is expected to encourage adherence and therapeutic benefits. They absorb sebum from the skin surface reduces oiliness which is the most common complaint regarding acne.

7) Solid lipid Nanoparticles

They are made from the solid lipid and they have a mean diameter of 50-1000nm. They are normally stabilized with lecithin. They are mainly synthesized with the use of synthetic or natural polymers and they are suited for the use in optimized delivery of drugs and reduce the toxicity of the drug. The maximum effect and use of nanoparticles for a certain drug solely depend on its ability to penetrate through the several anatomical barriers sustained release of the contents and its stability in the nanometric size. Their application in clinical medicine is limited because of its high-cost value and the scarcity of safe polymers with regulatory affairs [43]. To deal with this an alternative carrier is introduced which contains lipids mainly for the lipophilic pharmaceuticals. SLNs are the colloidal carrier which is developed for the alternative carrier system [44]. They are said to be the new generation of sub-micron sized lipid emulsion in which the liquid lipid (oil) is replaced by solid lipid that is why the name Solid Lipid Nanoparticles. They have unique properties like the smaller size, larger surface area, and high drug load [45,46].

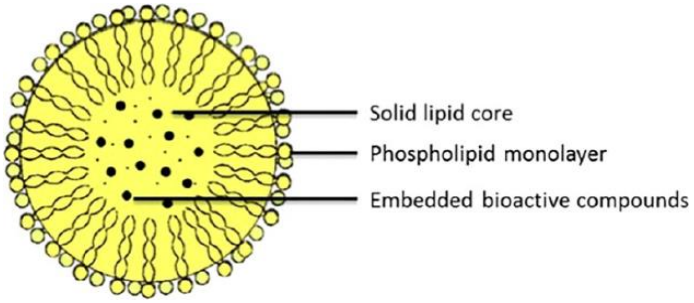

Fig. 11: Structure of Solid Lipid Nanoparticle

https://www.researchgate.net/figure/Schematic-illustrations-of-SLN-structure-Adapted-and-modified-from-ref-100_fig12_289489013

Advantage of SLN

The rate of release is solely depending upon the presence of the drug in the solid matrix. If the drug is placed in outer covering only, there will be no controlled release and if the moiety is homogeneously distributed within the lipid matrix the controlled release can be reached.

Disadvantage of SLN

Sometimes unexpected gelation can occur, unexpected dynamics, and polymeric transitions.

8) Hydrogel

They are the web of polymeric chains which is insoluble in water and they can also be found as a colloidal gel. They are super absorbent. They are swollen with water polymeric material that maintains a 3-Dimensional structure. They were the first biomaterials introduced for the use of the human body [47]. The novel approaches in hydrogel have revitalized the field of biomaterial research [48,49].

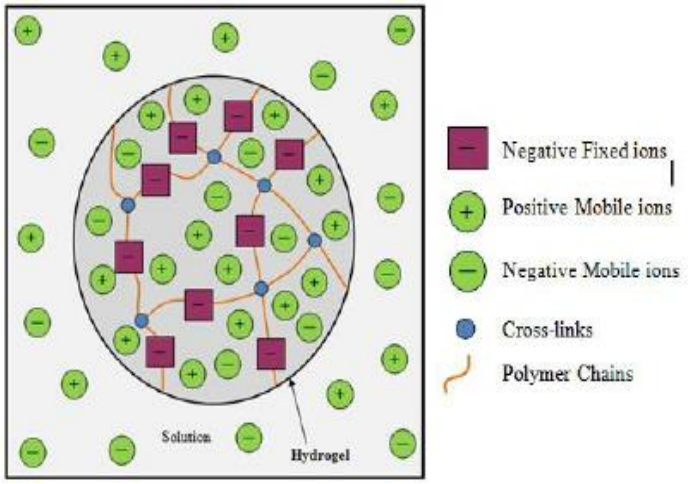

Fig. 12: Structure of Hydrogel

https://www.researchgate.net/figure/Hydrogel-structure-The-hydrogel-consist-of-cross-linked-chains-fixed-ions-and-contain_fig1_286354084

Advantage of Hydrogel

They can hold a huge quantity of water or biological liquids due to their 3-D structure and hydrophilic networks. Due to this property, the hydrogels show good biological applications.

9) Aerosol Foams

They are the products that are packed under highly pressurized containers with active ingredients that are used upon the activation of a valve. They are novel carrier systems used to apply on the hairy surface on the body like chest, back, etc.

Advantage of Aerosol foams

They maintain the required properties like moisturizing quick drying effects or higher bioavailability. Gas pressurized is used to dispense the aerosol foam.

10) Fullerenes

They are mainly composed of Carbon and when exposed to skin, they move through the skin within the cells, as opposed to moving through the skin. Works of literature on these have shown that they can be tolerated and can hold a substantial position in dermatologic and cosmetic uses.

Advantage of Fullerenes

The fullerenes are safe materials used for the suppression of Acne Vulgaris. They have great antioxidant properties. The inhibition of lipid peroxidation occurs fullerene's antioxidant property and sebum production is suppressed without any side effects.

11) Lipospheres

They are the lipid-based encapsulation system and is used as a topical drug delivery system for various medications. They consist of water-dispersible solid micro-particles and have the diameter that ranges between 0.1 to 100 µm. In the liposphere, the core is a solid hydrophobic lipid that is stabilized by the layers of phospholipid molecules embedded on their surfaces, that works as penetration enhancers.

Advantage of Liposphere

The stability is good, dispersibility in the aqueous medium is high, and prolonged release of various drugs including anti-inflammatory compounds, antibiotics, local anesthetics, and anti-cancer agents may use this type of system.

12) Polymers

They are large molecules that consist of repeating basic units of monomer which are connected by covalent bonds. The release of the active component in a single application is seen if the formulation contains a solution of a gel-like hydrophilic compound and a lipophilic compound in the form of suspension. In the future there a chance of developing bacterial therapy to overcome the problem of an antibiotic such as bacterial resistance. It is also possible to enhance the use of micro or Nanocarrier-based drug delivery system which can amplify the effectiveness of the treatment.

13) Nanostructured Lipid Carries (NLC)

They are the second-generation drug carrier system that is smarter and have a solid matrix at room temperature. They are made up of biocompatible, biodegradable and physiological lipid materials and surfactants and is accepted by the authorities for the use in drug delivery system of various types.

Advantage of NLCS

The drug loading tendency is enhanced, prevention of drug expulsion, and a more flexible structure for modulation of drug release.

14) Cyclodextrin Based Carriers

They are the type of the cyclic oligosaccharides extracted from the starch that contains six (alpha-CD), seven (beta-CD), eight (gamma-CD), or more (alpha-1,4)-linked alpha-D-glucopyranose units. The use of cyclodextrin complexation is a known technique for amplifying the solubility and drug stability, sustaining the release, and minimizes the deterioration of formulation by light. The main concern of investigation includes the combination of cyclodextrin complexation (dual approach) which may help in enhancing solubility, skin permeation, deposition, and reducing the degradation of drugs by light.

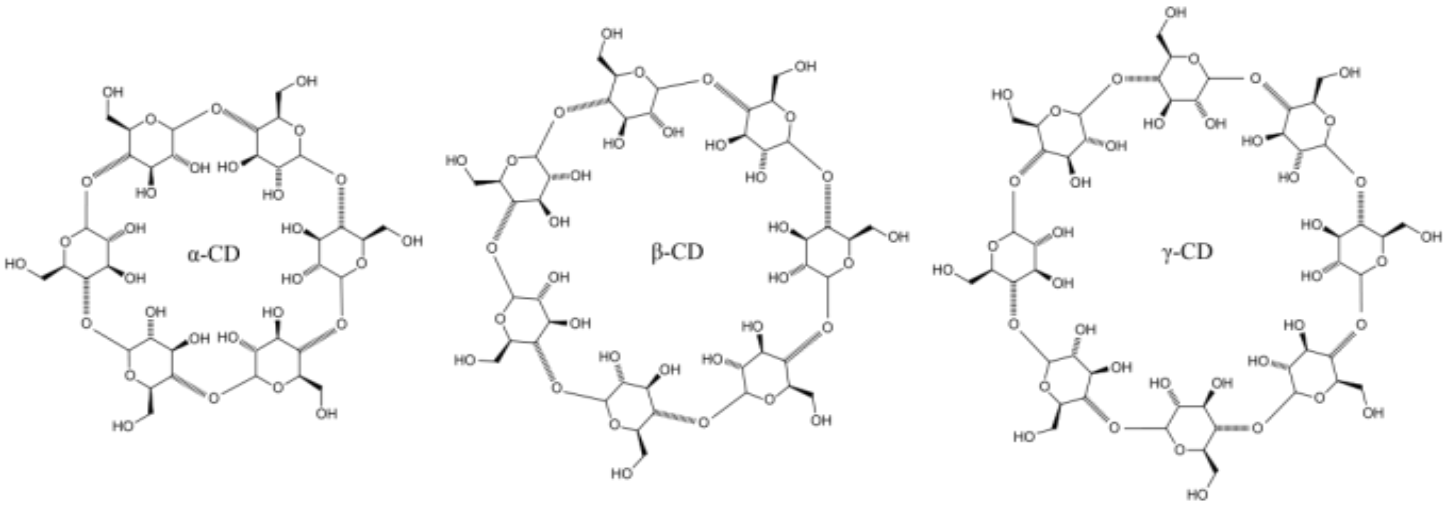

Fig. 13: Chemical structures of Cyclodextrins. https://www.researchgate.et/figure/Chemical-structure-of-cyclodextrins-Cyclodextrins-are-of-three-types-a-cyclodextrin_fig5_259156217

CONCLUSION

The adolescent stage is a complex life cycle characterized by physical, biological, social, and psychological changes. In this period the self-esteem of a person is developed, whereas conditions like anxiety, depression, or any other problem which may require medical advice can lead to a decrease in self-esteem. The visible changes in the acne can decrease self-esteem or it can affect a person psychologically or it can also hinder the quality of life of teenagers. The traditional oral and topical treatment has already shown their effectiveness regarding treating the acne, the commonness of the disease, and its resistant nature makes the development of new therapies highly required. The development regarding treating the acne is significant but not all the development is highly desirable. A topical formulation must be effective as it should be stable and amplified penetration of the actives at their concentration of efficacy; it should be acceptable and easily affordable and should not have its side effects.

ACKNOWLEDGEMENT

The authors would like to thank Amity Institute of Pharmacy, Amity University, Lucknow Campus for providing the library facilities for the review work.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Vyas A, Kumar Sonker A, Gidwani B. Carrier-based drug delivery system for treatment of acne. The scientific world journals. 2014;2014.
2. Enshaieh S, Jooya A, Siadat AH, Iraji F. The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: a randomized, double-blind placebo-controlled study. Indian Journal of Dermatology, Venereology, and Leprology. 2007 Jan 1;73(1):22.
3. Lin H, Xie Q, Huang X, Ban J, Wang B, Wei X, Chen Y, Lu Z. Increased skin permeation efficiency of imperatorin via charged ultradeformable lipid vesicles for transdermal delivery. International journal of nanomedicine. 2018; 13:831.
4. Abdel-Messih HA, Ishak RA, Geneidi AS, Mansour S. Tailoring novel soft Nano-vesicles 'Flexosomes' for enhanced transdermal drug delivery: Optimization, characterization and comprehensive ex vivo–in vivo evaluation. International journal of pharmaceutics. 2019 Apr 5; 560:101-15.
5. Tadwee IK, Gore S, Giradkar P. Advances in topical drug delivery system: a review. Int. J. of Pharm. Res. & All. Sci. 2012;1(1):14-23.
6. Alomrani AH, Badran MM. Flexosomes for transdermal delivery of meloxicam: characterization and antiinflammatory activity. Artificial cells, nanomedicine, and biotechnology. 2017 Feb 17;45(2):305-12.
7. El-Nabarawi MA, Shamma RN, Farouk F, Nasralla SM. Dapsone-Loaded Invasomes as a Potential Treatment of Acne: Preparation, Characterization, and In Vivo Skin Deposition Assay. AAPS PharmSciTech. 2018 Jul 1;19(5):2174-84.
8. Jang YH, Lee KC, Lee SJ, Kim DW, Lee WJ. HR-1 Mice: A new inflammatory acne mouse model. Annals of dermatology. 2015 Jun 1;27(3):257-64.
9. Vats A, Sharma P. Formulation and evaluation of topical anti acne formulation of coriander oil. International Journal of Pharmacy and Pharmaceutical Science Research. 2012;2(3):61-6
10. Ascenso A, Salgado A, Euletério C, Praça FG, Bentley MV, Marques HC, Oliveira H, Santos C, Simões S. In vitro and in vivo topical delivery studies of tretinoin-loaded ultradeformable vesicles. European Journal of Pharmaceutics and Biopharmaceutics. 2014 Sep 1;88(1):48-55.
11. Fitz-Gibbon S, Tomida S, Chiu BH, Nguyen L, Du C, Liu M, Elashoff D, Erfe MC, Loncaric A, Kim J, Modlin RL. Propionibacterium acnes strain populations in the human skin microbiome associated with acne. Journal of Investigative Dermatology. 2013 Sep 1;133(9):2152-60.
12. Jain AK, Jain A, Garg NK, Agarwal A, Jain A, Jain SA, Tyagi RK, Jain RK, Agrawal H, Agrawal GP. Adapalene loaded solid lipid nanoparticles gel: an effective approach for acne treatment. Colloids and Surfaces B: Biointerfaces. 2014 Sep 1; 121:222-9.
13. Dash M, Chiellini F, Ottenbrite RM, Chiellini E. Chitosan—A versatile semi-synthetic polymer in biomedical applications. Progress in polymer science. 2011 Aug 1;36(8):981-1014.
14. Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery–a review of the state of the art. European journal of pharmaceutics and biopharmaceutics. 2000 Jul 3;50(1):161-77.
15. Chen H, Chang X, Weng T, Zhao X, Gao Z, Yang Y, Xu H, Yang X. A study of microemulsion systems for transdermal delivery of triptolide. Journal of controlled release. 2004 Aug 27;98(3):427-36.
16. Amselem S, Friedman D, inventors; Pharmos Corp, assignee. Solid fat nanoemulsions as drug delivery vehicles. United States patent US 5,576,016. 1996 Nov 19.
17. Akbarzadeh A, Rogaie-Rezaei Sadabady, Davaran S, Joo Woo S, Zarghami N, Hanifehpour Y, Samiei M, Kouhi M, Kazem Nejati-Koshki. Liposome: classification, preparation, and applications. Nanoscale Research Lett. 2013; 8(1): 102. doi: 10.1186/1556-276X-8-102.
18. Kazi Masud K, Mandal Sattwa A, Biswas N, Guha A, Chatterjee S, Behera M, Kuotsu K. Niosomes: A future of targeted drug delivery systems. Journal of Advanced Pharmaceutical Technology and Research. 2010 Oct-Dec; 1(4): 374-380. doi: 10.4103/0110-5558.76435.
19. Kaity S, Maiti S, Ghosh AK, Pal D, Ghosh A, Banerjee S. Microsponges: A novel strategy for drug delivery system. Journal of Advanced Pharmaceutical Technology and Research. 2010 Jul-Sep; 1(3): 283-290. doi: 10.4103/0110-5558.72416.
20. Malhotra M, Jain NK, Niosomes as drug carriers. Indian Drugs. 1994; 31:81-6.
21. Udupa N. Niosomes as drug carriers. In: Jain NK, editor. Controlled and novel drug delivery. 1st edition. New Delhi: CBS Publishers and Distributors; 2002.
22. Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. The preparation and properties of Niosomes-Non-ionic surfactant vesicles. J Pharm Pharmacol. 1985; 37:863-8.
23. Brewer JM, Alexander J. The adjuvant activity of non-ionic surfactant vesicles (niosomes) on the BALB/c humoral response to bovine serum albumin. Immunology. 1992; 75:570-5.
24. Moser P, Marchand-Arvier M, Labrude P, Handjani-Vila RM, Vignerson C. Haemoglobin niosomes. I. Preparation, functional and physic-chemical properties, and stability. Pharma Acta Helv. 1989; 64:192-202.
25. Moser P, Arvier MM, Labrude P, Vignerson C. Niosomes of haemoglobin. II. Vitrointeractions with plasma proteins and phagocytes. Pharm Acta Helv. 1990; 65:82-92.
26. Hu C, Rhodes DG. Proniosomes: A Novel Drug Carrier Preparation. Int J Pharm. 1999; 185:23-35.

27. Hunter CA, Dolan TF, Coombs GH, Baillie AJ. Vesicular systems (Niosomes and Liposomes) for delivery of sodium stibogluconate in experimental murine visceral leishmaniasis. J Pharm Pharmacol. 1988; 40:161-5.
28. Sahoo SK, Labhasetwar V. Nanotech approaches to drug delivery and imaging. DDT. 2003; 8:24.
29. Gazibon A, Goren D, Cohen R, Barenholz Y. Development of liposomal anthracyclines: from basics to clinical applications. J control Release. 1998; 53:275-279. doi 10.1016/S0168-3659(97)00261-7.
30. Allen TM. Liposome. Opportunities in drug delivery. Drugs. 1997;54(Suppl 4):8-14.
31. Johnston MJ, Semple SC, Klimuk SK, Ansell S, Maurer N, Cullis PR. Characterization of the drug retention and pharmacokinetic properties of liposomal nanoparticles containing dihydrosphingomyelin. Biochim Biophys Acta. 2007:1768:1121-1127 doi. 10.1016/l.bbamen.2007.01.019.
32. Hofheinz RD, Gnad Vogt SU, Beyer U, Hochhaus A. Liposomal encapsulated anti-cancer drugs. Anticancer Drugs. 2005; 16:691-707. doi: 10.1097/01.cad.0000167902.53039.5a.
33. Nacht S, Kantz M. The microsponge; A novel topical programmable delivery system. Top Drug Deliv Syst. 1992; 42:299-325.
34. Badawi AA, Nour SA, Sakran WS, El-Mancy SMS. Preparation and Evaluation of Microemulsion Systems Containing Salicylic Acid. AAPS PharmSciTech. 2009 Dec; 10(4): 1081-1084. doi: 10.1208/s12249-009-9301-7.
35. Collier K, Matalonis S, Owen AJ. Evaluation of permeability enhancement by microemulsion in a caco-2 cell system. Proc Int Symp Control Release Bioact Mater. 1999; 26:5444.
36. Alany RG, Rades T, Agatonovic-Kustrin S, Dvies NM, Tucker IG. Effects of alcohols and diols on the phase behavior of quaternary systems. Int J Pharm. 2000; 196:141–145. doi: 10.1016/S0378-5173(99)00408-1.
37. Trotta M, Pattarino F, Grosa G. Formation of lecithin-based microemulsions containing n-alkanol phosphocholines. Int J Pharm.1998; 174:253–259. doi: 10.1016/S0378-5173(98)00273-7.
38. Marti-Mestres G, Nielloud F. Emulsions in health care applications—an overview. J Dispers Sci Technol. 2002; 23:419–439.
39. Osborne DW, Ward AJ, O'Neill KJ. Microemulsions as topical drug delivery vehicles: in-vitro transdermal studies of a model hydrophilic drug. J Pharm Pharmacol Comm. 1991; 43:451–454.
40. Jachowicz J, Berthiaume MD. Microemulsions vs. macroemulsions in hair care products. Cosmet Toiletries. 1993; 108:65–72.
41. Jaiswal M, Dudhe R, Sharma PK. Nanoemulsion: an advanced mode of drug delivery system. 3 Biotech. 2015 Apr; 5(2): 123-127. doi: 10.1007/s13205-014-0214-0.
42. Hossain KMZ, Patel U, Ahmed I. Development of microspheres for biomedical applications: a review. Prog Biomater. 2015 Mar: 4:1-19. doi: 10.1007/s40204-014-0033-8.
43. Scheffel U, Rhodes BA, Natajaran TK, Wagner HN. Albumin microspheres for study of the reticuloendothelial system. J Nucl Med.1970; 13:498–503.
44. Jumaa M, Muller BW. Lipid emulsions as a novel system to reduce the haemolytic activity of lytic agents: Mechanism of protective effect. Eur J Pharm Sci. 2000; 9:285–90.
45. Cavalli R, Caputo O, Gasco MR. Solid lipospheres of doxorubicin and idarubicin. Int J Pharm. 1993;89: R9–R12.
46. Mukherjee S, Ray S, Thakur RS. Solid Lipid Nanoparticles: A modern Formulation Approach in Drug Delivery system. Indian J Pharm Sci. 2009 Jul-Aug; 71(4): 349-358. doi: 10.4103/0250-474X.57282.
47. Wichterle O, Lím D. Hydrophilic gels for biological use. Nature. 1960;185:117–118.
48. Kopeček J, Yang J. Hydrogels as smart materials. Polym Int. 2007.
49. Kopeček J. Hydrogels Biomaterials: A smart future? Biomaterials. Author manuscript; available in PMC 2008 Dec 1. doi: 10.1016/j.biomaterials.2007.07.044.
50. Liao DC. "Management of acne," Journal of Family Practice, vol. 52, no. 1, pp. 43–51, 2003.
51. Leydon J. "Comparing facial tolerability of a 3-step acne system containing a novel solubilized 5% benzoyl peroxide lotion for normal to dry skin with that of a benzoyl peroxide/clindamycin combination prescription product," Journal of the American Academy of Dermatology, vol. 58, supplement 2, no. 2, p. 15,2008.
52. Thiboutot D. Jarratt M. Rich P. Rist T. Rodriguez D. and Levy S. "A randomized, parallel, vehicle-controlled comparison of two erythromycin/benzoyl peroxide preparations for Acne vulgaris," Clinical Therapeutics, vol. 24, no. 5, pp. 773–785, 2002.
53. Wang F. Kwak HS. Elbuluk N. et al., "Retinoic acid 4-hydroxylase inducibility and clinical response to isotretinoin in patients with acne," Journal of the American Academy of Dermatology, vol. 61, no. 2, pp. 252–258, 2009.
54. Gabriels M. Brisaert M. and Plaizier-Vercammen J. "Densitometricthin layer chromatographic analysis of tretinoin and erythromycin in lotions for topical use in acne treatment," European Journal of Pharmaceutics and Biopharmaceutics, vol.48, no. 1, pp. 53–58, 1999.
55. Spellman MC and Pincus SH. "Efficacy and safety of azelaic acid and glycolic acid combination therapy compared with tretinoin therapy for acne," Clinical Therapeutics, vol. 20, no. 4, pp. 711–721, 1998.
56. Verschoore M, Poncet M. Czernielewski J. Sorba V. and Clucas A, "Adapalene 0.1% gel has low skin-irritation potential," Journal of the American Academy of Dermatology, vol. 36, no. 6, supplement, pp. S104–S109, 1997.
57. Shalita AR. Berson DS. Thiboutot DM et al., "Effects of tazarotene 0.1% cream in the treatment of facial acne vulgaris: pooled results from two multicenter, double-blind, randomized, vehicle-controlled, parallel-group trials," Clinical Therapeutics, vol. 26, no. 11, pp. 1865–1873, 2004.

58. Xu Y. Yang X. and Xu X, "Preparation and evaluation of tea tree oil liposome," West China Journal of Pharmaceutical Sciences, 2006.
59. Rougier A and Richard A, "Efficacy and safety of a new salicylic acid derivative as a complement of vitamin A acid in acne treatment," European Journal of Dermatology, vol. 12, no. 4, pp.49–50, 2002.
60. Yaroshinsky A and Leyden J. "The safety and efficacy of clindamycin [1% as clindamycin phosphate and tretinoin (0.025%)] for the treatment of acne vulgaris: a combined analysis of results from six controlled safety and efficacy trials," European Journal of Dermatology, vol. 50, no. 3, p. 23, 2004.
61. Vermeulen B. Remon JP. and Nelis H. "The formulation and stability of erythromycin-benzoyl peroxide in a topical gel," International Journal of Pharmaceutics, vol. 178, no. 1, pp. 137–141, 1999.
62. Lucky AW. Maloney JM. Roberts J et al., "Dapsone gel 5% for the treatment of acne vulgaris: safety and efficacy of long-term treatment," Journal of Drugs in Dermatology, vol. 6, no. 10, pp.981–987, 2007.
63. del Rosso JQ. "The use of sodium sulfacetamide 10%-sulfur5% emollient foam in the treatment of acne vulgaris," Journal of Clinical and Aesthetic Dermatology, vol. 2, no. 8, pp. 26–29,2009.

How to cite this article:
Singh N, Singh M and Panwar S. An overview on Novel Drug Delivery Systems for Acne. *Int. J. Res. Dev. Pharm. L. Sci.* 2019; 8(4): 1-12. doi: 10.13040/IJRDPL.2278-0238.8(4).1-12