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Review Article

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NOVEL DRUG DELIVERY SYSTEM AND ITS USE IN THE TREATMENT OF ACNE

M.Jothish*, Pranitha, kundana, G.Sarath Chandra Reddy.

Vignan Institute of Pharmaceutical sciences, Deshmukhi, Nalgonda.

E-mail: jotish1@gmail.com

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Abstract:

Acne is a cutaneous pleomorphic disorder of the pilosebaceous unit involving abnormalities in sebum production and is characterized by both inflammatory (papules, pustules and nodules) and noninflammatory (comedones, open and closed) lesions. Propionibacterium acnes and Staphylococcus epidermidis are common pus-forming microbes responsible for the development of various forms of acne vulgaris. Common therapies that are used for the treatment of acne include topical, systemic, hormonal, herbal and combination therapy. Topically used agents are benzoyl peroxide, antibiotics and retinoids. Systemically used agents are antibiotics and isotretinoin. These drugs produce a number of potential side effects and development of resistance to frequently used antibiotics. Novel Drug delivery system plays a crucial role in curing ACNE. **Having Optimum concentration of drug molecules and direct citation of drug to the site of action helps in curing ACNE** with out side effects and there by the efficacy of the drug is increased by involvement of the Nano Particles. This review focuses on the treatment of **ACNE VULGARIS** using **NOVEL DRUG DELIVERY SYSTEM**.

Key Words: Acne Vulgaris, Novel Drug Delivery System, Benzoyl Peroxide.

INTRODUCTION:

ACNE Vulgaris:

Acne is the term for plugged pores (blackheads and whiteheads), pimples, and even deeper lumps (cysts or nodules) that occur on the face, neck, chest, back, shoulders and even the upper arms. Acne vulgaris (commonly called acne) is a skin condition caused by changes in the pilosebaceous units. Acne is most common during adolescence, affecting more than 85% of teenagers, and frequently continues into adulthood. For most people, acne diminishes over time and tends to disappear. The majority of the acne sufferers exhibit mild to moderate acne initially, which progresses to the severe form in certain cases. Typical acne lesions are comedones, inflammatory papules, pustules and nodules. Some of the large nodules were previously called "cysts" and the term *nodulocystic* has been used to describe severe cases of inflammatory acne.

CAUSES OF ACNE :

- Genetically..... There is a much greater chance for the children to have acne if their parents had acne in their teenage years, as the genes carry information from the parents to children. This form of acne cannot be avoided until and unless the advancement of medical sciences leads to the deletion of the culprit genes.
- Hormonal..... There is production of the androgen hormones during the adulthood years and this hormone activates the stimulation of the oil producing glands in the skin and this leads to the clogging of the pores and in turn results in the causation of pimples and blackheads.
- Stress..... This is not a proven fact whether the stress causes the initiation and formation of acne lesions, but this can surely aggravate the acne pimples and can also aggravate any condition of the skin that you are suffering from.

- Diet.....: It is not surely known that the diet can cause the formation of acne pimples as is the case with stress, but there are some experts who believe that the allergies to certain foods can cause the trigger of the acne problem in an individual.
- Other factors..... Hyperactive sebaceous glands
Due to some species of bacteria like *Propionibacterium acnes* (*P. acnes*)
Use of anabolic steroids
Chemical compounds particularly exposure to dioxins.

STAGES IN THE ACNE:

1. Acne develops as a result of blockages in follicles.
2. Hyperkeratinization and formation of a plug of keratin and sebum is the earliest change.
3. Enlargement of sebaceous glands and an increase in sebum production occur.
4. Commensal bacteria *Propionibacterium acnes* can cause inflammation, leading to inflammatory lesions in the dermis.

ILLUSTRATION:



Image representing Acne vulgaris scattered on face and neck.

TREATMENTS:

1.Topical therapy:

Topical therapy is employed as first-line treatment in mild acne, whereas for moderate and severe acne, systemic therapy is required in addition to topical therapy. Currently, several topical agents are available that affect at least one of the main pathogenetic factors responsible for the development of acne.

The conventional creams and lotions fail to obviate the problems enumerated because the creams and lotions are excessively greasy and have the potential to sequester the active ingredient so that the percutaneous absorption of the drug and its efficacy is reduced. Although topical therapy has an important position in acne treatment, side effects associated with various topical antiacne agents and the undesirable physicochemical characteristics affect their utility and patient compliance.

The local side effects, however, mainly cutaneous irritation, erythema, dryness, peeling and scaling, remain major problems. Novel vesicular and particulate drug delivery systems have been proposed to reduce the side effects of drugs commonly used in the topical treatment of acne.

2. Hormonal Treatment :

In females, the common combined estrogen/progestogen methods of hormonal contraception have some effect, but the antiandrogen, Cyproterone, in combination with an oestrogen (Diane 35) is particularly effective at reducing androgenic hormone levels.

3. With Retinoids :

Topical retinoids such as tretinoin (brand name Retin-A), adapalene (brand name Differin), and tazarotene (brand name Tazorac). Like isotretinoin, are related to vitamin A, but they are administered as topicals and generally have much milder side effects. They can, however, cause significant irritation of the skin.

A daily oral intake of vitamin A derivative isotretinoin can cause long-term resolution or reduction of acne.

4. Sulfur:

Sulfur has an inhibitory effect on the growth of *Propionibacterium acnes* and, when combined with sodium sulfacetamide

5. Dermabrasion :

Dermabrasion is procedure in which the surface of the skin is removed by abrasion. It is used to remove sun-damaged skin and to remove or lessen scars and dark spots on the skin.

These treatments, though common, offer less efficacy and hence, there arises a need for a targeted drug delivery for effective cure of the disease.

Novel drug delivery system and its use in treatment ACNE:

The method by which a drug is delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all. On the other hand, the very slow progress in the efficacy of the treatment of severe diseases, has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. To minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone, various drug delivery and drug targeting systems are currently under development. Novel drug delivery strategies can play a pivotal role in improving the topical delivery of antiacne agents by enhancing their dermal localization with a concomitant reduction in their side effects.

This novel formulation helps by encouraging collagen production in the skin. It helps improve overall skin tone and luster and improves the appearance of fine lines. It is made of a combination of collagen and Hyaluronic acid.

Light, oil-free lotion contains finely milled prescription-grade medicinal agents to heal blackheads and blemishes and helps prevent future breakouts. The advanced delivery system in Repairing Lotion is soothing and safe for entire face.

Novel Topical Delivery Systems:

Targeting is the ability to direct the drug-loaded system to the site of interest. Controlled drug release and subsequent biodegradation are important for developing successful formulations.

Potential release mechanisms involve:

- (i) Desorption of surface-bound /adsorbed drugs;
- (ii) Diffusion through the carrier matrix;
- (iii) Diffusion (in the case of nanocapsules) through the carrier wall;
- (iv) Carrier matrix erosion; and
- (v) A combined erosion /diffusion process.

1. AEROSOL FOAMS:

Aerosol foams have become an increasingly popular type of topical formulation for a variety of skin conditions including acne vulgaris. The vehicle base of the foam can have a liquid or semi-solid consistency that shares the same physicochemical characteristics of conventional vehicles like creams, lotions and gels, but it maintains desirable properties such as moisturizing/ fast-drying effects, or higher drug bioavailability. The aerosol base is dispensed through a gas-pressurized can that discharges the foam. The product characteristics (i.e., texture, bubble size and thickness, viscosity, density, persistence, stability, and spreadability) are determined by the type of formulation and the dispensing container that are selected to suit the specific treatment needs. In acne, foams may be preferred for application on large hairy surfaces (e.g., chest and back) or on the face as cleansers, because they are easier to apply.

2. LIPOSOMES:

Liposomes are frequently used as vehicles in pharmaceuticals and cosmetics for a controlled and optimized delivery to particular skin layers. Liposomes are spherical vesicles whose membrane consists of amphiphilic lipids (i.e., lipids that are hydrophilic on one side and lipophilic on the other side) that enclose an aqueous core, similar to the bilayer membranes of living cells. Because liposomes offer an amphiphilic environment, they may encapsulate hydrophilic substances in their aqueous core and lipophilic substances in their lipid bilayer. This unique dual release capability enables the delivery of two types of substances once they are applied on the skin; each differs in its effects on skin permeability, which may enhance the desired therapeutic benefit.

3. NANOEMULSIONS:

Nanoemulsions are a class of emulsions (i.e., water-in-oil or oil-in-water formulations) that are characterized by the dispersion of very small-sized droplets when mixed. Nanoemulsions are not formed spontaneously, as they require unique thermodynamic conditions, specialized manufacturing processes, and specific surfactants that can stabilize the nano droplets. Nanoemulsions are suitable for the transport of lipophilic compounds into the skin and, therefore, they may be an ideal vehicle for use in acne to increase the penetration of the active compounds inside the lipophilic environment of the pilosebaceous unit. In addition, nanoemulsion particulates will not clog the pores and they can produce additional therapeutic effects, such as increased skin hydration and viscoelasticity.

4. POLYMERS:

Polymers are large molecules consisting of repeating structural units, or monomers that are connected by covalent chemical bonds. These compounds serve as the building blocks of natural (e.g., paper and amber), biological (e.g., proteins and nucleic acid), or synthetic (e.g., plastics and

polyethylene) materials. Today, applications for synthetic polymers can be found in nearly every industry, and their versatility has given rise to technological advancements within the pharmaceutical sector that address a variety of medical needs. For example, in dermatology, there are new acrylic-acid polymers that turn into a gel in the presence of water by trapping water into microcells. Inside these aqueous microcells, hydrophilic compounds can remain in a solution, where as non-hydrophilic compounds may be dispersed in suspension. The result is a stable gel-like formulation that is easy to use and releases the active compounds once they are applied on the skin. Moreover, these polymer-based gels can be mixed with other excipients, such as moisturizers and emollients, to provide additional clinical benefits.

Recently introduced anti-acne formulations that combine clindamycin 1% with benzoyl peroxide 5% utilize this novel polymer-based gel technology that exhibits efficacy and excellent tolerability.

5. MICROSPONGES:

Microsponges are biologically inert particles that are made of synthetic polymers with the capacity to store a volume of an active agent up to their own weight. Furthermore, the particles serve to protect the entrapped active compound from physical and environmental degradation. The microsphere technology can be utilized in a variety of formulations, but is more frequently manufactured as gels. Once applied on the skin, microsponges slowly release the active agents.

6. EMULSIFIER FREE FORMULATIONS:

Emulsifier-free formulations are also a growing area of development for dermatologic and cosmetic products. Most skin care products are emulsions, i.e., a mixture of two or more materials that

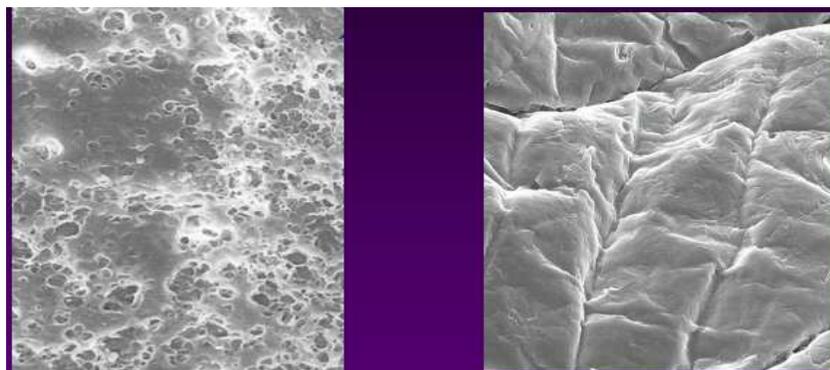
are not miscible with each other; as such, according to the second law of thermodynamics, they are inherently unstable. As a result, they require the addition of surfactants (emulsifiers) that stabilize the formulation to guarantee an adequate shelf life. Furthermore, once these surfactant agents are applied on the skin, they tend to emulsify and remove the natural lipids of the epidermis. Consequently, the pharmaceutical industry has been developing surfactant-free emulsions as alternatives to conventional formulations by using stabilizers, such as polymeric emulsifiers or solid particles, in order to yield sufficiently stable products with a cosmetically pleasant appearance.

7. FULLERENES:

Fullerenes are molecules composed entirely of carbon that resemble a hollow sphere. Once fullerenes come into contact with the skin, they migrate through the skin intercellularly, as opposed to moving through cells. Therefore, a fullerene could be used to 'trap' active compounds and then release them into the epidermis once they are applied on the skin. Moreover, fullerenes, themselves, are thought to be potentially potent antioxidants. Data are reported in the literature showing that fullerenes are well tolerated and they hold substantial promise in dermatologic and cosmetic applications.

USE OF BENZOYL PEROXIDE IN ACNE TREATMENT:

A new and improved topically applied pharmaceutical preparation for the treatment of acne and an improved vehicle for delivering the active ingredients thereof to the human skin in a manner whereby the bioavailability and percutaneous absorption of the active ingredient is remarkably enhanced. The vehicle comprises a volatile silicone, a fatty alcohol having from 12-22 carbon atoms, benzoyl peroxide; and such preservatives or emulsifying agents. Benzoyl peroxide when effectively incorporated into the present delivery system exhibits improved stability, and enhanced bioavailability.



Insoluble Benzoyl Peroxide

Soluble Benzoyl peroxide (Novel Drug)



Benzoyl Peroxide Cream

RESULTS & DISCUSSIONS:

Much progress has been made to improve the performance of topical anti-acne care products in recent years. New excipients, refined processing techniques, and a better knowledge of the physicochemical properties of vehicles and drugs have led to the development of new delivery systems that may result in more advanced anti-acne therapies. Well controlled clinical trials will be required to confirm the clinical benefits of these new formulations in terms of efficacy, tolerability, compliance, and cosmetic acceptability.

The encapsulation of antiacne drugs in vesicular and particulate delivery systems represents an innovative alternative to minimize side effects, while preserving their efficacy. This can be obtained by the capacity of these systems to provide controlled release or to improve the drug penetration into skin or even into the pilosebaceous unit.

For a proper and effective novel drug delivery, certain specifications regarding the product stability have to be given much importance. In this case, depending on the properties of the combined ingredients, a dispensing container will be chosen (i.e., tube, jar, can, etc.) to provide a stable physicochemical environment that protects the active compounds from chemical degradation. In the same way, an efficacious anti-acne formulation should facilitate the penetration of the active compounds into the skin more fastly with increased rate of absorption.

In today's self-image conscious world, patients are looking for topical products that are not only safe and effective, but also cosmetically acceptable and easy to apply. This is especially true in acne, where the aesthetic aspect is one of the primary reasons why patients seek dermatologic consultation. Moreover, acne patients are mainly comprised of teenagers or young adults, and therefore, products that offer convenience and are minimally disruptive to daily routines increase the level of compliance, and ultimately, the efficacy of the topical therapy.

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Current Author Address:

M.Jotish*,

Vignan Institute of Pharmaceutical Sciences,

Dehsmukhi, Nalgonda Dist.