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To Development of a Noveltopical Drug Delivery System

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ABSTRACT

The paper reviews an overview of a conventional and novel approach in the topical drug delivery system. This drawback overcomes by extensive research to develop a novel topical drug delivery systems targeting to improve the safety, efficacy and to minimize side effects. The conventional review focuses on dusting powders, poultices, plasters, lotion, liniments, solution, emulsion, suspension, colloidions, tinctures, creams, gels, ointments, pastes, suppositories, transdermal delivery systems, tapes, and gauzes and rubbing alcohol while the novel review focuses on novel gels, aerosol foams, microsponges, muco-adhesive bio-adhesives, novel vesicular carriers, nano-emulsion &nano-emulgel, protein and peptide delivery, polymers, emulsifier-free formulations and fullerenes etc. The key purpose of a topical delivery system is to enhance the skin permeability and to retain in the dermis. This review addresses a basis for further advancement and up-gradation of current techniques and technologies

Introduction:

Dermal products applied topically are categorized based on those applied to produce local effects and systemic effects. The paper reviews an overview of a conventional and novel approach in the topical drug delivery system. Drug delivery via the skin is becoming progressively popular due to its convenience and affordability. The skin is the most important mechanical barrier to the penetration of many drug substances and acts as an ideal site to deliver the drug both locally and systemically. The topical route has been a favored route of drug administration over the last decades. Despite conventional topical drug delivery systems limits in poor retention and low bioavailability. This drawback overcomes by extensive research to develop a novel topical drug delivery systems targeting to improve the safety, efficacy and to minimize side effects. The conventional review focuses on dusting powders, poultices, plasters, lotion, liniments, solution, emulsion, suspension, colloidions, tinctures, creams, gels, ointments, pastes, suppositories, transdermal delivery systems, tapes, and gauzes and rubbingalcohol while the novel review focuses on novel gels, aerosol foams, microsponges, muco-adhesive bio-adhesives, novel vesicular carriers, nano-emulsion &nano-emulgel, protein and peptide delivery, polymers, emulsifier-free formulations and fullerenes etc. The key purpose of a topical delivery system is to enhance the skin permeability and to retain in the dermis. This review addresses a basis for further advancement and up-gradation of current techniques and technologies.

Dermal products applied topically are categorized based on those applied to produce local effects and systemic effects. These systems are generally used for local skin infections whereas other route of drug administration.

Drug molecules with low doses delivered through topical route effectively that are limited to a small area anywhere in the body. Stratum corneum is lipid-rich in nature composed of 40% lipids, 40% protein, and only 20% water. Lipophilic character of the drug is best suited for topical delivery whose transport is aided by dissolution into intercellular lipids around the cells of the stratum corneum. However, hydrophilic drugs are difficult to transport to the stratum corneum layer because of its low water content. These molecules are absorbed into the skin through "pores" or openings of the hair follicles and sebaceous glands that restricts drug absorption.

Topical drug delivery systems skin serves as one of the most easily accessible routes for drug administration. Stratum corneum has been regarded as the major barrier to penetration of substances in to and through the skin. However, the presence of stratum corneum on the surface makes it selective towards applied drugs or delivery systems. Topical delivery is defined as the application of pharmaceutical dosage form to the skin for direct treatment of cutaneous disorder or the cutaneous manifestation of the general.

Context:

Strategy of dual therapy has been proposed to minimize the amount of each drug and to achieve the synergistic effect for cancer therapies.

Objective:

The aim of this study was to develop an effective drug delivery system for the simultaneous topical delivery of two anti-tumor agents, cisplatin and imiquimod.

Material and methods:

The preformulation studies were carried out in terms of tests for identification, solubility profile, determination of partition coefficient and simultaneous estimation of both drugs by UV-Visible spectrophotometer and High Performance Liquid Chromatography (HPLC). Drug-drug and drug-excipients interactions were examined by thin layer chromatography, infrared spectroscopy, differential scanning calorimetry (DSC) and X-ray diffraction (XRD). Provesicular drug delivery system (protransfersome gel formulation) have been prepared and characterized by in vitro and in vivo parameters.

Review and Literature:

The paper reviews an overview of a conventional and novel approach in the topical drug delivery system. Drug delivery via the skin is becoming progressively popular due to its convenience and affordability.The paper reviews an overview of a conventional and novel approach in the topical drug delivery system.The conventional review focuses on dusting powders, poultices, plasters, lotion, liniments, solution, emulsion, suspension, colloidions, tinctures, creams, gels, ointments, pastes, suppositories, transdermal delivery systems, tapes, and gauzes and rubbing alcohol while the novel review focuses on novel gels, aerosol foams, microsponges, muco-adhesive bio-adhesives, novel vesicular carriers, nano-emulsion &nano-emulgel, protein and peptide delivery, polymers, emulsifier-free formulations and fullerenes etc. The key purpose of a topical delivery system is to enhance the skin permeability and to retain in the dermis. This review addresses a basis for further advancement and up-gradation of current techniques and technologies

Importance:

Topical formulations for pharmaceutical delivery are becoming increasingly popular. Topical delivery has a number of advantages: the ability to deliver drug substance more selectively to a specific site, avoiding fluctuations in drug levels, inter- and intra-patient variations, improved compliance, and an enhanced suitability for self-medication. Skin provides an ideal site for the delivery of drug substances for both local and systemic effects. However, it also acts as a mechanical barrier to the penetration of many drug substances.

With topical therapies, the formulation is as important as the molecule itself because the interaction of the vehicle with the skin can alter the efficacy of the penetrant. The formulation ensures that the drug substance is delivered to the right target site and that it maintains dosage integrity, drug transport, and active duration

For example, the drug substance in a psoriasis treatment may have some efficacy simply from the hydrating or soothing effects of the formulation. Whether the molecule maintains purity, potency, and delivery to the right target site may be masked by the ingredients that surround it. Both the mechanical barrier properties of the top layer of skin, stratum corneum, and the physicochemical properties of the drug affect the transportation of the drug substance from formulation vehicle to the site of action.

The Right Combination of Drug/Excipients:

The selection of the right excipients for topical formulations is extremely important. The drug substance may be efficacious, but its interaction with excipients may alter the following:

• Its ability to permeate through skin

• Its stability through shelf life

• Its ability to not metabolize in skin
• Its ability to stay dissolved at right concentrations
• Its capability to achieve desired release rates
For a recently developed topical formulation, Tergus optimized an emulsion cream to dissolve the drug up to a certain concentration. The excipients were chosen to optimize the solubility of the drug substance and to prevent oil and water phase separation. However, a change in formulation to increase the drug concentration, so it could accommodate the toxicology study requirement, resulted in phase separation due to inadequate emulsifiers. The formulation was redone to optimize the concentration of emulsifiers, as well as the addition of a viscosity-building excipient. A non-homogenous cream could have resulted in erroneous toxicology outcomes.
For another project, Tergus worked with a novel molecule that had undergone preformulation, solubility, and selection of excipients. Analysis showed drug substance degradation and increasing impurity levels. Forced degradation studies were performed to prove which kind of degradation was affecting the molecule.
It was discovered the drug was undergoing oxidative degradation in the formulation. Steps were taken to prevent oxidation through the careful selection of excipients, limit exposure to atmosphere, and minimize drug degradation. Investigation into the root causes were conducted and found that trace levels of peroxides were in one of the excipients. Early stage development used the same excipient in a pure grade, so oxidation was not prevalent. During scale-up, another supplier of the same excipient was chosen, and this particular supplier's material had low levels of peroxides which degraded the drug substance.

Advantages:

- Incorporation of hydrophobic drugs
- Better loading capacity
- Better stability
- Controlled release
- No intensive sonication
- Avoiding first pass metabolism
- Avoiding gastrointestinal incompatibility
- More selective for a specific site
- Improved patient compliance
- Convenient and easy to apply 7

Disadvantages:

- Skin irritation on contact dermatitis
- The possibility of allergenic reactions
- The poor permeability of some drugs through the skin
- Drugs of large particle size are not easy to absorb through the skin

LOCAL ROUTES:
Topical Drug delivery
Topical drug delivery systems skin serves as one of the most easily accessible routes for drug administration. Stratum corneum has been regarded as the major barrier to penetration of substances in to and through the skin. However, the presence of stratum corneum on the surface makes it selective towards applied drugs or delivery systems.

Topical Drug delivery:

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FACTORS MODIFYING DRUG ACTION:

Topical Drug delivery

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NEWDRUGDEVELOPMENT:

Topical Drug delivery

Topical drug delivery systems skin serves as one of the most easily accessible routes for drug administration. Stratum corneum has been regarded as the major barrier to penetration of substances in to and through the skin. However, the presence of stratum corneum on the surface makes it selective towards applied drugs or delivery systems.The major steps/stages in the development.Topical drug delivery systems skin serves as one of the most easily accessible routes for drug administration. Stratum corneum has been regarded as the major barrier to penetration of substances in to and through the skin. However, the presence of stratum corneum on the surface makes it selective towards applied drugs or delivery systems.activity in the right compound; rarely employed now.Lead optimization A more practical approach is tosynthesize chemical congeners of natural products/syntheticcompounds with known pharmacological activity in the hopeof producing more selective/superior drugs. Many familiesGrades of strength of evidenceGrade I Systematic reviews/Meta-analysis Most reliable, may form the basis ofclinical decisionsGrade II Well powered randomized Reliable, but may be supported orcontrolled trial/more than one trials refuted by similar studiesGrade III Open label trials/pilot studies/ Less reliable, need more rigorous testing,observational (cohort and case-control) may indicate further investigationstudies (prospective or retrospective)Grade IV Case reports/anecdotal reports/ Least reliable; may serve as pointersclinical experience to initiate formal studiesStages in new drug development

- Synthesis/isolation of the compound: (1–2 years)
- Preclinical studies: screening, evaluation, pharmacokinetic and short-term toxicity testing in animals: (2–4 years)
- Scrutiny and grant of permission for clinical trials: (3–6 months)
- Pharmaceutical formulation, standardization of chemical/biological/immuno-assay of the compound: (0.5–1 year)
- Clinical studies: phase I, phase II, phase III trials; long-term animal toxicity testing: (3–10 years)
- Review and grant of marketing permission: (0.5–2 years)
- Postmarketing surveillance: (phase)

Results:

The mean size, poly dispersity index (PDI) and zeta potential of transfersomal vesicles formed by protransfersome hydration were 429.5 nm, 0.631 and -68.1 Mv, respectively. The prepared formulation showed toxicity on cutaneous squamous cell carcinoma cell line (A-431) at 200 µg (cisplatin) and 1 mg (imiquimod) concentration of drug in combination against control. The cisplatin- and imiquimod-loaded provesicular dual-drug delivery system achieved an optimal antitumor effect, increase in lifespan, antiviral, and toxicity reduction, revealing the advantage of site specific drug delivery and the modified combination therapy.

Discussion:

Cisplatin delivery through protransfersome gel in combination with imiquimod may potentiate the activity against solid tumors of epidermal origin.

Conclusion:

Data revealed that combination therapy considerably enhances antitumor efficacy of the drug for skin-cited malignancies.

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