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Design and Characterization of Flucytosine Loaded Bioadhesive In Situ Ophthalmic Gel for Improved Bioavailability

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Abstract

Flucytosine is a semisynthetic macrolide antibiotic used for the treatment of trachoma caused by *Chlamydia trachomatis*, a gram negative bacteria. The study was planned to formulate in situ ocular gel of Flucytosine to prolong the pre-corneal residence time and gives the better bioavailability as compare to conventional dosage form. The in situ gel of Flucytosine was prepared by mixing with polymer of xanthan gum, HPMC and sodium alginate in different ratio. The six different formulations were prepared and evaluated for Clarity, visual appearance, pH, gelling capacity, drug content, in vitro drug release, kinetic model and ocular irritancy. The best formulation was subjected for stability study. The results of evaluation parameters were satisfactorily for all formulations, while F4 demonstrated maximum drug release at 8 hr and follow zero order drug release. The findings of ocular irritant indicates the F4 were non irritant and safe to use. The outcomes of stability study indicate that the F4 gel stored at room temperature and accelerated temperature were found to be comparatively stable. The study concluded that the in situ ocular gel of Flucytosine will be substitute for conventional eye drops in future.

1 Introduction

Ophthalmic ointments guarantee unrivaled drug bioavailability by expanding the contact time, limiting the dilution by tears, and opposing nasolacrimal drainage. Significant impediment of ointment, giving obscured vision, because of this it could be utilized either evening or for treatment outwardly and edges of the eyelids. Suspension as ophthalmic delivery systems relies on the assumption that particles may persist in conjunctival sac. Precorneal drug loss can be minimal, for example, hindering waste by utilizing dispersion controlled, nonerodible polymeric insert. The significant detriment of inserts is the lack of of patient acknowledgment inferable from difficult administration. The improvement of more up to date, increasingly sensitive diagnostic techniques and therapeutic agents render criticalness to the advancement of progressively fruitful ocular delivery systems. The primitive ophthalmic solution, suspension, and ointment dosage forms are unmistakably no longer adequate to battle these ailments, and flow innovative wor current research and development efforts to configuration better therapeutic systems are the essential focal point of this exploration work.

In this way, these might be overwhelmed by fabricating the drug as a formulation that undergoes instantaneous in situ gel formation upon ophthalmic administration. They experience gelation after instillation because of physical-chemical changes occurring in the eye. It increases the pre-corneal residence time and better bioavailability of drug can be achieved by accomplished in situ gel[1-3].

Flucytosine is a semisynthetic macrolide antibiotic utilized for the treatment of trachoma caused by *Chlamydia trachomatis*, a gram negative bacteria. As indicated by WHO, there are around 84,000,000 individuals who had been influenced by trachoma. It is accounted for that the existent oral dosage forms of Flucytosine are suitable to treat the ocular infections for example, conjunctivitis and others brought about by delicate pathogens. But when Flucytosine is taken orally to cure ocular infection, it needs at least 1.0 g Flucytosine per dose to ensure the drug content in aqueous humor, tear fluid and conjunctival coat reach

Antimicrobial and Antifungal Activity of Newly Synthesized 4-Hydroxy Quinoline Derivatives

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Abstract

The synthesis of 4- Hydroxy quinolin-2-one derivatives by three deferent synthetic pathways and the formyl substitution on the 3 rd position one heterocyclic quinoline ring. The Schiff base reaction reacts with 4-Hydroxy-3-formylquinolin-2-one and form twelve different derivatives by using four different hydrazine derivatives. These derivative show satisfactory antimicrobial and anti fungal activity. The newly synthesized compounds were screened for their antibacterial activity against B. subtilis, S. aureus, E.coli and K. pneumonia by cup plate method. A control was also prepared for the plates in the using solvent DMSO. Activity of each compound was compared with ciprofloxacin as standard. The newly synthesized compounds were also screened for their antibacterial activity against A. nige and C. albicans by cup plate method. A control was also prepared for the plates in the using solvent DMSO. Activity of each compound was compared with Griseofulvin as standard. The investigation of antibacterial and antifungal screening data revealed that all the tested compounds and showed moderate to good inhibition at 50-100 µg/ml in DMSO. The compound P1-a, P1-b, P2-a, P2-b, P3-a and P3-c showed comparatively very good activity against all the bacterial strains. The good activity is attributed to the presence of pharmacologically active phenyl hydrazones and semicarbazone on position 3 on quinoline ring. Presence of phenyl group on the position-1 also increases the antimicrobial activity. A new series of Substituted 4-Hydroxy quinoline-2-one derivatives have been synthesized. The research study reports the successful synthesis and antimicrobial activity of new 4-Hydroxy-3-substituted-1-H/Methyl/Phenylquinolin-2-one carrying biologically active groups. Their antimicrobial activity study revealed that all the compounds tested showed moderate to very good antibacterial and antifungal activities against pathogenic strains.

***Key Word**: 4-Hydroxy Quinoline, Hydrazones, Antimicrobial activity, Antibacterial*

INTRODUCTION

Quinoline is the bicyclical compound, which give a verity of pharmacological activity. The quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmacological properties. Quinine was isolated as the active ingredient from the bark of Cinchona trees and successively replaced the crude bark for the malaria therapy. Despite its relatively low efficacy and

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REVIEW ARTICLE

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Emerging Trends in Ocular Drug Delivery Special Reference to *In Situ* Ophthalmic Gel

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Abstract

Eye is the most complex and valuable organ of the body, because of its prompt pre-corneal elimination of dosage form. In order to overcome this, researchers developed a new system; in-situ gel forming system. This formulation undergoes phase transition in the eye to form gel, thus prolonging the precorneal contact time which will result in improved visual bioavailability. There are different novel ocular drug delivery systems such as In-situ gel, dendrimers, niosomes, nanoparticulate system, collagen shield, ocular iontophoresis suspension and ocusert etc. This framework comprises of polymer or mixture of polymers which display sol-gel transition due to physicochemical parameters (temperature, ion exchange & pH) of the body. This novel drug delivery system promotes the importantly ease and convenience of administration, deliverance of accurate dose as well as to prolong residence time of drug in contact with mucosa. This review incorporates different temperature, pH, and ion induced in situ-forming polymeric systems used to achieve prolonged contact time of drugs with the cornea and increment their bioavailability.

1 Introduction

Ophthalmic preparations are characterized in the USP as "sterile dosage forms, basically free from foreign particles, suitably compounded and stuffed for instillation into the eye." In eye medicate is controlled at various site for example, cornea, conjunctiva and sclera for better achievement of bioavailability and required impacts related with the therapy. The drugs for allergies, glaucoma, bacterial infections, conjunctivitis, keratitis, local anaesthetics and viral infection can be administered at suitable sites in the eye[1].

2 Ocular drug delivery system

Among the different courses of drug delivery, the field of ophthalmic drug delivery is one of the most interesting and challenging endeavours facing a pharmaceutical researcher.

The anatomy, physiology and biochemistry of the eye render this organ incredibly impermeable to foreign substances[2]. A noteworthy issue of ocular drug delivery is not the lack of efficient drugs but the attainment of their optimal concentration at the required site of action[3]. The most significant and well-acknowledged route of administration for the treatment of different eye disorders is the topical instillation of drugs through eye drops. Conventional pharmaceutical formulations, such as solutions, suspensions and ointments have many disadvantages –

- Rapid precorneal elimination due to tear turnover
- Frequent instillation
- Enzymatic metabolism
- Nasolacrimal drainage
- Conjunctival absorption
- Blurred vision
- Absence of controlled release[4]

In spite of these impediments, noteworthy improvements have been made in ocular drug delivery. several new strategies for drug delivery are made which are equipped for controlling the rate of drug delivery, sustaining the duration of therapeutic activity or targeting the delivery of the drug to a tissue. These

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Review Article

Emulgel: A Topical Preparation

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ABSTRACT

Emulgel is an emerging topical drug formulation which is becoming increasingly popular due to its advantages over the conventional topical preparations. The emulgel is a combination of an emulsion and a gel and thus has a dual release control system. Its biggest and most favorable advantage has been the ability to incorporate hydrophobic drugs, thus making it emerge as a more popular choice these days. The emulgel is also greaseless, transparent; it can be easily spread and removed, has a long shelf- life, is thixotropic and is also pleasant looking. The emulgel is turning out be a preferred choice for cosmetic and dermatological preparations and its use and application will accelerate in the coming future.

KEYWORDS: Emulgels, hydrophobic drugs, topical drug delivery.

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INTRODUCTION

A topical drug is delivered or applied on the surface of the human body such as the skin or the mucous membrane via a vast extent of classes including creams, foams, gels, lotions, and ointments.[1]They are applied on a very large scale spectrum of both cosmetic and dermatological applications that can be for healthy as well as diseased skin.[2] Drug substances are rarely administered alone, but somewhat as a part of a formulation, in combination with one or more non - medicated agents that serve different and specialized pharmaceutical function. Some topical administrations are applied on the skin but they actually work towards being absorbed systemically.[3]Drug absorption through the skin is augmented if we have the drug substance in the solution form or if the lipid/water partition coefficient is favorable and the last criteria could be that it is a non- electrolyte. Antiseptics, antifungal agents, skin emollients and protectant are some of the type of drugs which are used for their localized actions. There are many advantages of tropical drug delivery systems such as avoidance of first pass metabolism and gastrointestinal incompatibility. Their major advantage being that they increase patient compliance and the patient can easily self- administer these medications without any dependence on another person. They also have short biological half- life and a slight therapeutic window and thus can easily be stopped when required.[4, 5]

Human skin is a unique organ that allows the terrestrial life to regulate its heat and water loss from the body and at the same time it also prevents the entry of harmful chemicals or microorganisms. The skin is the largest organ of the human body and covers almost 10% of the total body surface and approximately covers an average area of 1.7 m^2. Being such a large and easily accessible organ, the skin has many ideal as well as multiple sites to administer therapeutic agents for both local and systemic actions. The human skin is also a very highly efficient self- repairing barrier to the contaminants of the outside and it keeps the insides of the human body inside and separate from these external parameters.[6]

Gels are semi- solid preparations which have varying properties such as being soft and weak to hard and tough.[7] Gels are considerably dilute cross- linked system, which do

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Review Article

Farmer's Lungs Disease: It's Take A Breath Away!

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ABSTRACT

Farmers were evaluated for the presence of farmer's lung disease by serologic methods and by clinical histories. Farmer's lung disease (FLD) is a form of hypersensitivity pneumonitis (HP) caused by inhaling microorganisms from hay or grain stored in conditions of high humidity in the agricultural workplace. The epidemiology of the disease is not well known, and is based on studies conducted by Central European and Asian groups. The clinical presentation may vary, differentiating the chronic (exposure to lower concentrations of the antigen over a longer period time) and the acute forms (after exposure to high concentrations of the antigen). It is more common in middle-aged men, although this probably reflects differences in exposure levels. It is also more common in non-smokers, probably because tobacco reduces the IgG response to inhaled antigens, affects cytokine production, and alters macrophage function. The etiology of the disease is clear - the inhalation of mouldy hay dust - and much can be done to prevent it ifthis is borne in mind. Mouldy hay dust is a very complex material consisting of innumerable fungal spores, hyphae and bacteria and fragments of vegetable matter. The treatment of FLD is based mainly on avoiding exposure to the antigen. This is the only measure that has been shown to delay disease progression. Corticosteroids are traditionally recommended in patients with impaired lung function and beta agonist and alpha blockers are also helpful in the treatment of disease.

Keyword: Farmer's lungsdisease(FLD), Hypersensitivity Pneumonitis(HP), Allergy, Dust.

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INTRODUCTION

Farmer's lung disease(FLD) is a form of hypersensitivity pneumonitis(HP). According to previous studies, the most common antigens are usually thermophilic actinomycetes and fungi. In patients with respiratory symptoms and agricultural occupational exposure, radiological, lung function and/or anatomical pathology findings must be compatible with FLD, bronchoalveolar lavage must Show lymphocytosis, and tests must find sensitivity to the antigen. The main treatment is avoidance of the antigen, so it is essential to educate patients on preventive measures. To date, no controlled studies have assessed the role of immunosuppressive therapy in this disease. Corticosteroid treatment has only been shown to accelerate resolution of the acute forms, but there is no evidence that it is effective in preventing disease progression in the long-term or reducing mortality.[1]

History

In 1713 Ramazzini' observed that grain handlers and farmers of the Po valley were troubled by lung diseases. The first modern mention of lung disease in farmers is attributed to Cadham1 in Winnipeg in 1924; he reported three From the respiratory section, department of medicine, University of Manitoba and the clinical investigation unit, St. Boniface General Hospital, Winnipeg Reprint requests to: Dr. C.P.W. Warren, Clinical investigation unit, St. Boniface General Hospital, 409 Tache Ave., Winnipeg, Man. R2H 2A6 cases of asthma after exposure to wheat rust (Puccinia graminis)[2].Bjornsson wrote that his grandfather, an Icelandic farmer, suffered from "heymaedi" (hay shortness of breath) in the early 19th century[3].