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Development and characterization of dexamethasone nanodispersion for the effective treatment of diabetic retinopathy

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ABSTRACT

Diabetic retinopathy is the most common complication of diabetes and remains the leading cause of vision loss worldwide. The potent glucocorticoid based anti-inflammatory drug dexamethasone (DEX) chosen for the present work is long-acting with half-life of 37–72 h extensively metabolized in to 6-hydroxy-dexamethasone (6-OH-DEX). The present work aimed to develop dexamethasone loaded nanodispersion (DEX-ND) by improving its solubility, half-life, and bioavailability in biological system thereby this formulation may be afforded economically. With the concept that polymeric surfactant improves the solubility of challenging water insoluble drug the present work has been hypothesized to improve its solubility using polyvinyl pyrrolidone (PVP-K30) polymer and polysorbate 80 (Tween 80) hydrophilic non-ionic surfactant, thereby the bioavailability is expected to get enhanced. By varying the PVP K30 and Tween 80 concentrations three different formulations were developed. The developed DEX-ND was further characterized for its compatibility, particle size, zeta potential, morphology, and *in vitro* release behavior. The results of Fourier transform infrared spectrometric analysis indicate the compatibility nature of DEX-ND along with other excipients/drug used in the formulation. The developed formulations showed spherical morphology, particle size ranging from 550.46 ± 107.82 to 3560 ± 284.29 nm, zeta potential ranging from −29.23 ± 1.09 to −7.793 ± 1.01 mV. The amount of DEX present in the DEX-NDs was found to be 0.95–3.93 mg. The *in vitro* release studies as performed by dialysis bag method showed a sustained release pattern. The results of *ex vivo* corneal permeation studies indicates that the developed DEX- NDs has some exposure to the posterior segment of the eye.

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1. Introduction

Nanodispersions are a dispersed form of nanoparticles accompanied with a size range of 100 nm or less than 100 nm.[1] Nanodispersion has the capacity to permeate the cornea.[2] They are stable in aqueous phase with emulsifiers accelerating its absorption. The preparation is carried out with the breakdown of drug in a volatile solvent.[3] Nanodispersions are commonly stored at 4 °C in a dispersed form.[4] Nanodispersion will increase the dissolution characteristics therefore enhance the saturation solubility.[5] Designation of products and aqueous media of lipophilic molecule solubilization is accompanied by nanodispersion.[6] Nanodispersion ability of transparency and stability improves ocular residence time, reduces precorneal loss with prolonged and controlled drug delivery.[7] Nanodispersions are prepared by several methods such as modified coacervation, ionotropic gelation,[8] solvent displacement, emulsion phase inversion, microfluidization, and high pressure homogenization The bioactive components of nanodispersion reduce the chances of particle aggregation and phase separation.[9,10] Nanodispersion enhance the bioavailability of drugs placed into the eye.[8]

Diabetic retinopathy (DR) is the most common complication of diabetes and remains the leading cause of vision loss globally.[11–13] Neovascularization resulting from excessive hypoxia is the hallmark of proliferative DR, in which vascular leakage causes due to the breakdown of blood retina barrier (BRB) which is considered to be the primary cause for the pathogenesis of diabetic macular edema (DME).[14,15] DR can be very broadly divided into two stages, depending on the degree of micro-angiogenesis and associated ischemic injury. DR is classified into two types, viz. non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) (micro-aneurysms in the retina).[11] The NPDR is characterized by increased production of various inflammatory mediators in the retina such as tumor necrosis factor α, nuclear factor KB, and intercellular adhesion molecule-I.[11] Vision loss occurs only in advanced stages and is characterized by DME and PDR.[11] Production of inflammatory and angiogenic mediators induce stress response in

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