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A green chemistry approach towards synthesizing hydrogel for sustained ocular delivery of brinzolamide: *In vitro* and *ex vivo* evaluation

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ABSTRACT

Brinzolamide is a carbonic anhydrase inhibitor used in the eye drop form for the treatment of glaucoma quires frequent dosing to attain therapeutic concentration. Therefore, this study aimed to prepare sustained drug delivery of brinzolamide. The objective of the study was to prepare a hydrogel loaded with a nanostru lipid carrier (NLC) of brinzolamide. The hydrogel was prepared by a green synthesis approach using genip natural crosslinking agent and polymers such as carboxymethyl chitosan and poloxamer 407. The emulsification-ultra sonication method was used to prepare a nanostructured lipid carrier of brinzolamide, was loaded into a hydrogel using a swelling and loading method. The NLC formulation has shown small p sizes of 111.20 ± 2.15 nm, polydispersity index of 0.280 ± 0.005 and % entrapment efficiency of 82.1 0.14%. The NLC-loaded hydrogels of brinzolamide formulations were studied for swelling properties and sl temperature and pH-responsive swelling behavior. The optimized hydrogel formulation has been studied *vitro* drug release and showed drug release for a longer duration (24 h) than marketed eye drops (8 h). In *vivo* study, hydrogel formulations showed transcorneal permeability 4.54 times greater than marketed eye The hydrogel formulation of brinzolamide produced by the green synthesis method has shown sustained-r properties with no sign of ocular irritation. Hence, the hydrogel of brinzolamide-loaded NLC would be t tential drug delivery approach in the near future for sustained ocular drug delivery in glaucoma manager

1. Introduction

The eye is an essential organ of the human system and is well known for typical anatomy and physiology [1]. It has the most complex, unique barrier, restricting entry to the most active substances [2]. Topical application of eye drop is a commonly used route in treating eye diseases. However, more than 90% of active drugs from eye preparations fail to cross the eye's corneal membrane due to nasolacrimal drainage, eye blinking, and lacrimation [3]. Therefore, ideal ocular delivery is warranted to improve not only corneal permeation but also precorneal residence time.

To overcome the bioavailability problem of conventional eye drops, several nanotechnology-based carriers have been designed. Polymeric nanoparticles [4], nanocrystals [5], liposomes [6], nanoemulsions [7], and nanostructured lipid carriers (NLCs) [8] have shown improvement in ocular bioavailability. NLCs are new generation carriers preferred over other nanocarriers because of its lipidic nature and biocompatibility with ocular membrane [9–11]. Its manufacturing materials are cost-effe easy to manufacture, and do not require organic solvents [9,1 However, NLC has less mucoadhesiveness and poorly adheres to th surface due to its less viscous nature [14–16]. Its consistency c improved by increasing its viscosity. NLC can be loaded into an *in s* or hydrogel system in order to improve ocular retention and bioavailability [17]. Due to less concentration and ocular irrit hydrogels are generally preferred over *in situ* gels [18–20].

Hydrogels are three-dimensional structured systems that can a several folds of water without losing their structural integrity [21]. polymeric hydrogels convert into their gel form in response to v conditions such as temperature, the presence of ions, and differe environments [22]. An interpenetrating polymer network (IPN) is of hydrogel in which a mixture of polymers is used, one of whic dergoes a crosslinking reaction. Due to their attractive mech properties, semi-IPN type polymeric hydrogels have been studie ocular use [23]. The hydrogel formed using single polymer compo

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