



1 Introduction:

The ocular drug delivery route is of great interest because of the ~~is one of the most important drug delivery routes. The eye has unique~~ physiological and physicochemical structures ~~found within the eye. that~~ Owing to such structures, ~~make this organ resistant to~~ eyes tend to resist the ~~permeation of drugs permeation,~~ meaning that certain substances must be administered to the eye (and retained by the eye) to ensure effective treatment. ~~For a treatment to be effective, sufficient quantities of active ingredients need to be delivered to and retained within the eye. Eye drops represent the most common ocular drug administration method~~ Eye drops are the most common dosage forms. However, ~~the~~ This method's most significant drawback is eye drops' low ~~y do not have suitable~~ bioavailability—~~roughly~~ after an eye drop is administered, approximately 70% of ~~it may be wasted~~ the administered drug does not reach its target. ^[1] Various anatomical and physiological barriers—for example, nasolacrimal drainage, the drug's inadequate time spent in the precorneal area, and low corneal permeability—~~represent t~~ The primary reasons for drugs' e poor bioavailability ~~when delivered ocularly~~ of drugs is largely due to anatomical and physiological barriers, including nasolacrimal drainage, short presence time in the precorneal area, and low corneal permeability. ^[2]

The cornea's ~~main~~ is a physical and chemical barrier, the primary purpose of which is to keep ~~protect~~ the eye's intraocular tissues ~~of the eye safe~~. The ~~corneal membrane of the cornea has a heterogeneous texture consisting of~~ comprises several layers, each with unique characteristics. These layers include the epithelium, stroma, and endothelium, with the first two playing significant roles in drug absorption. ~~,~~ and each layer of this membrane has different physicochemical characteristics. Among these layers, stroma and epithelium are the most important in terms of drug absorption. ~~It is not possible for d~~ Drugs compounds with high hydrophilic or lipophilic effects ~~cannot enter the~~ to pass through the corneas via passive transport. ~~as t~~ The stroma layer is a rate-limiting membrane for ~~water hating~~ hydrophobic drugs, whereas the epithelium layer is a rate-limiting membrane for ~~water loving~~ hydrophilic drugs. ^[3-5]

~~The impenetrability of the corneal epithelium layer and associated short retention time of drugs mean that~~ The drugs administered as eyedrops have poor corneal permeability ~~of drugs administered using ophthalmic drops is weak because of the short retention time and impenetrability of the corneal epithelium layer.~~ —Because of these challenges, oOcular

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31 nanocarriers (e.g., liposomes, micelles, solid lipid nanoparticles, and microemulsions) are used
32 can be classified to improve ocular drug delivery. as liposomes, micelles, solid lipid
33 nanoparticles, and microemulsions. [6-9]

34 Quercetin is a natural flavonoid that appears to have with low toxicity when administered orally
35 or intravenously. [10] that Quercetin has been intensively received significant attention from
36 researchers studied because of its owing to its anticancer, anti-inflammation, anticancer, and
37 antioxidant properties effects. [10+13] Quercetin Moreover, quercetin might help might be useful
38 for reducing the oxidative stress associated with eye complications, involved in the
39 formation of including senile cataracts, which is the most common age-related eye complication.
40 [14] The damage of as well as retinal epithelium related to age-related macular degeneration
41 (ADME), which causes retinal epithelium damage can be protected by quercetin. Quercetin
42 also promotes ROS-catalyzing protein expression, and therefore, protection mechanisms are
43 involved in the inhibition of might also help protect the eyes against pro-inflammatory factor (IL-
44 6) synthesis by inducing the expression of ROS-catalyzing proteins. [15] According to murine
45 uveitis models, this anti-inflammatory potential is related to quercetin's ability to. Additionally,
46 murine uveitis models indicate the anti-inflammatory potentials of quercetin in the suppress
47 retinal S antigen-induced of intraocular inflammation induced by retinal S antigen. [16]
48 However, the instability of of note, quercetin cannot be taken orally, as this delivery method
49 results in results in poor bioavailability and, poor permeability, and as well as extensive
50 considerable first-pass metabolism when administered orally. [12]