Application of membrane-active peptide-based therapeutics in the management of stromal melts associated with microbial keratitis

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ABSTRACT

Advanced **microbial keratitis** causes corneal ulceration and stromal melts. An imbalance of matrix metalloproteinases (MMPs) and exogenous collagenases or other enzymes released by the infecting pathogen degrades corneal tissue. It causes **tissue damage resulting in blindness**. No targeted treatments exist to stop corneal melting. An **antimicrobial peptide targeting the cornea** of anterior eye was designed. With its **collagen interaction properties**, it is anticipated to be a promising agent for preventing microbial keratitis-induced stromal melts.

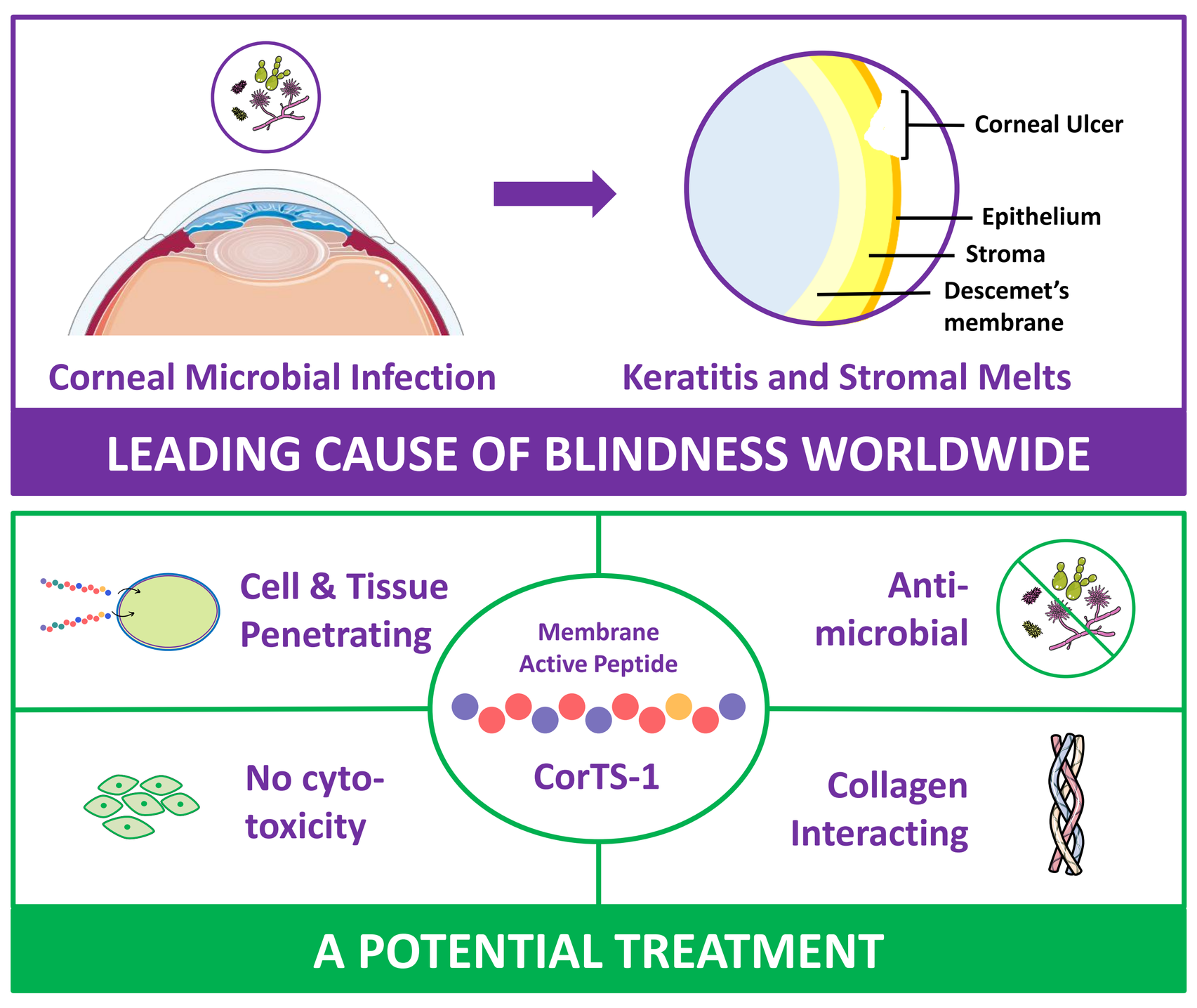

Fig. 1. Graphical abstract

METHODOLOGY

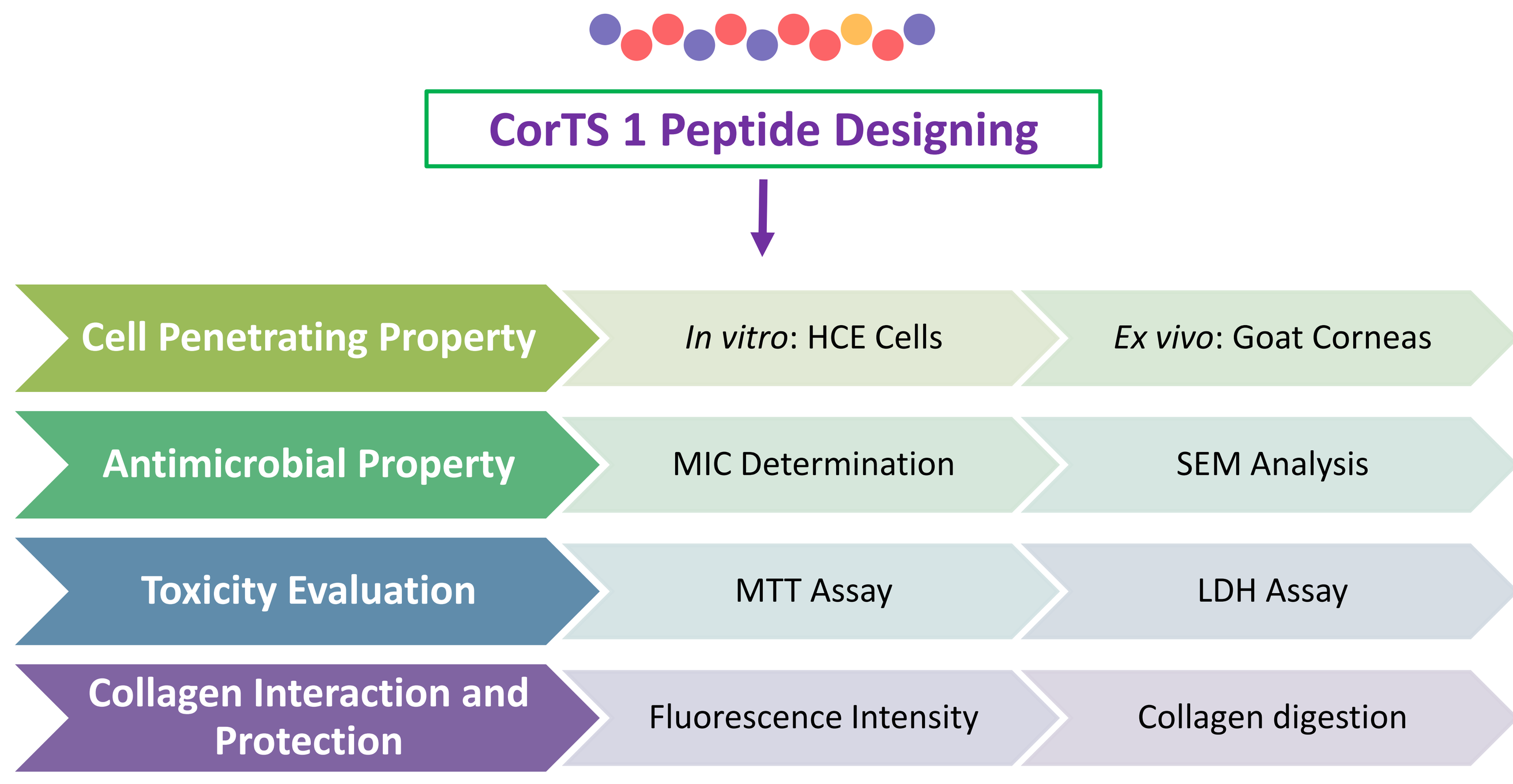

Fig. 2. Summarized methodology

RESULTS

1. Cell Penetrating Property

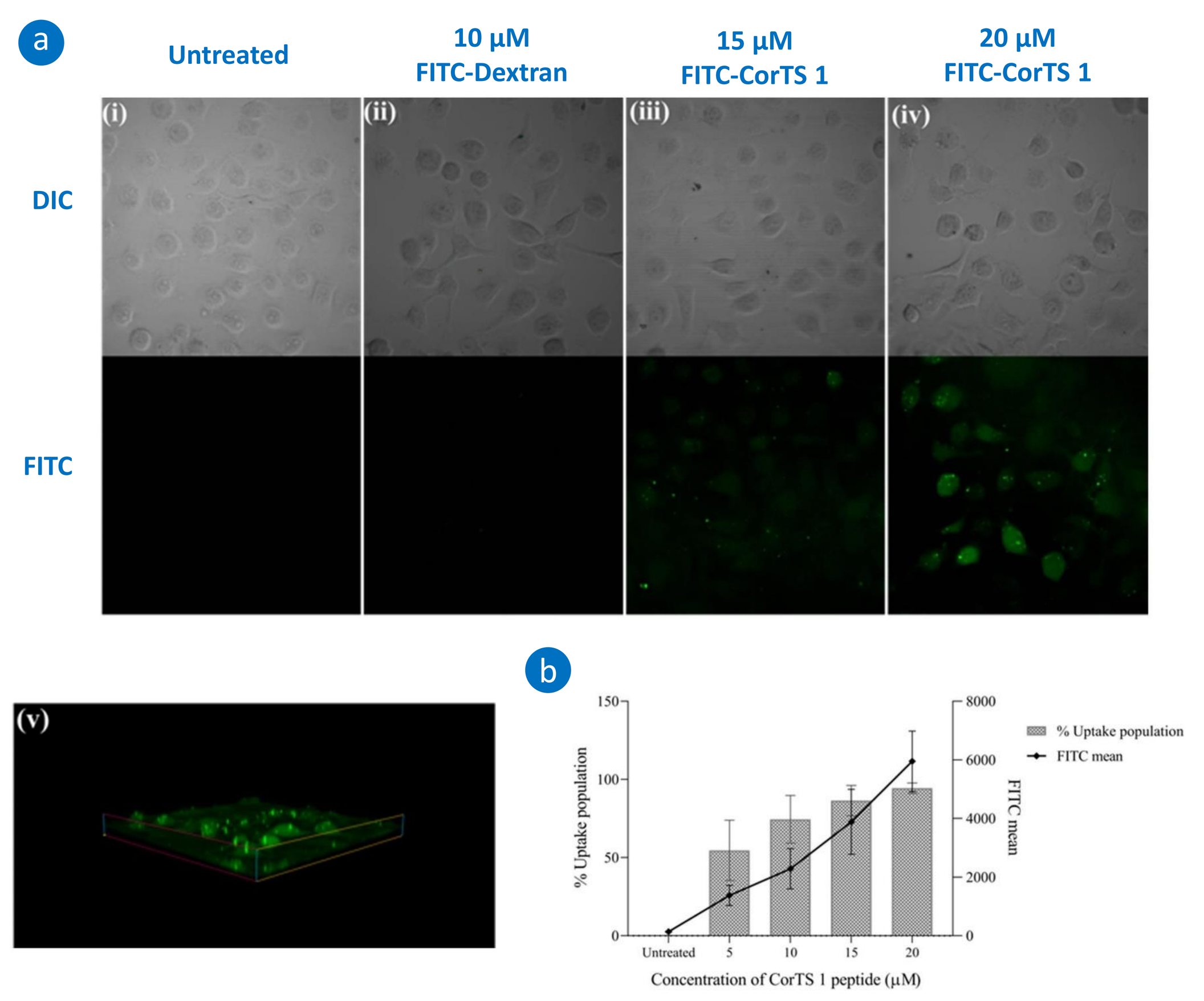

Fig. 3. (a) Confocal microscopy of (i-iv) CorTS 1 uptake on HCE cells (v) a z-section image of HCE cells treated with 20 µM FITC CorTS 1, (b) Percentage uptake population and FITC mean of HCE cells treated with CorTS 1 as measured by flow cytometry.

2. Peptide- Collagen Interaction

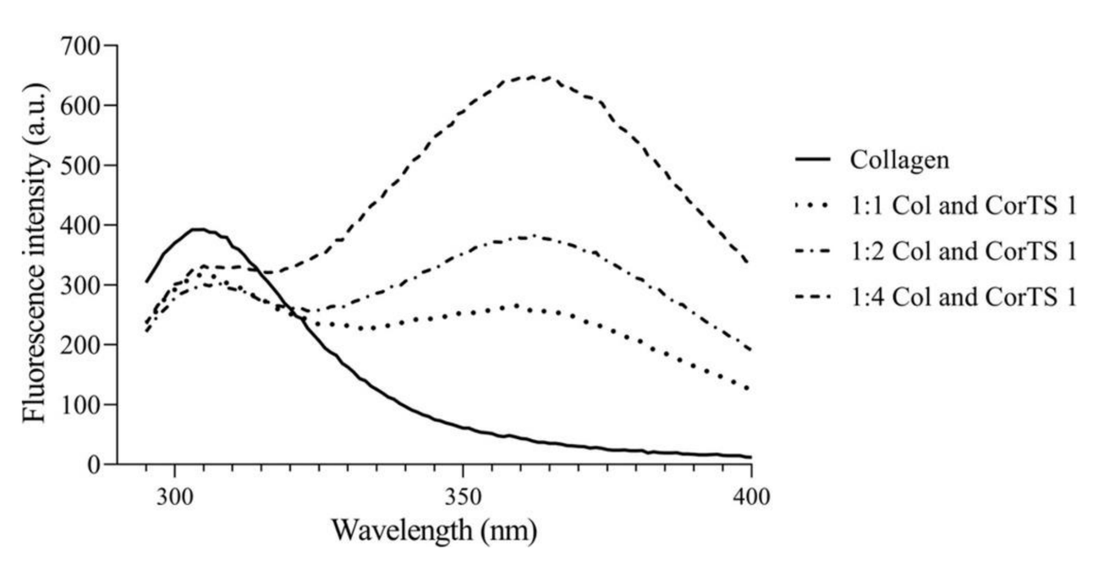

Fig. 4. Fluorescence emission spectra of 5 µM Collagen alone and in presence of CorTS 1 at different ratios.

3. Anti-microbial Property Investigation

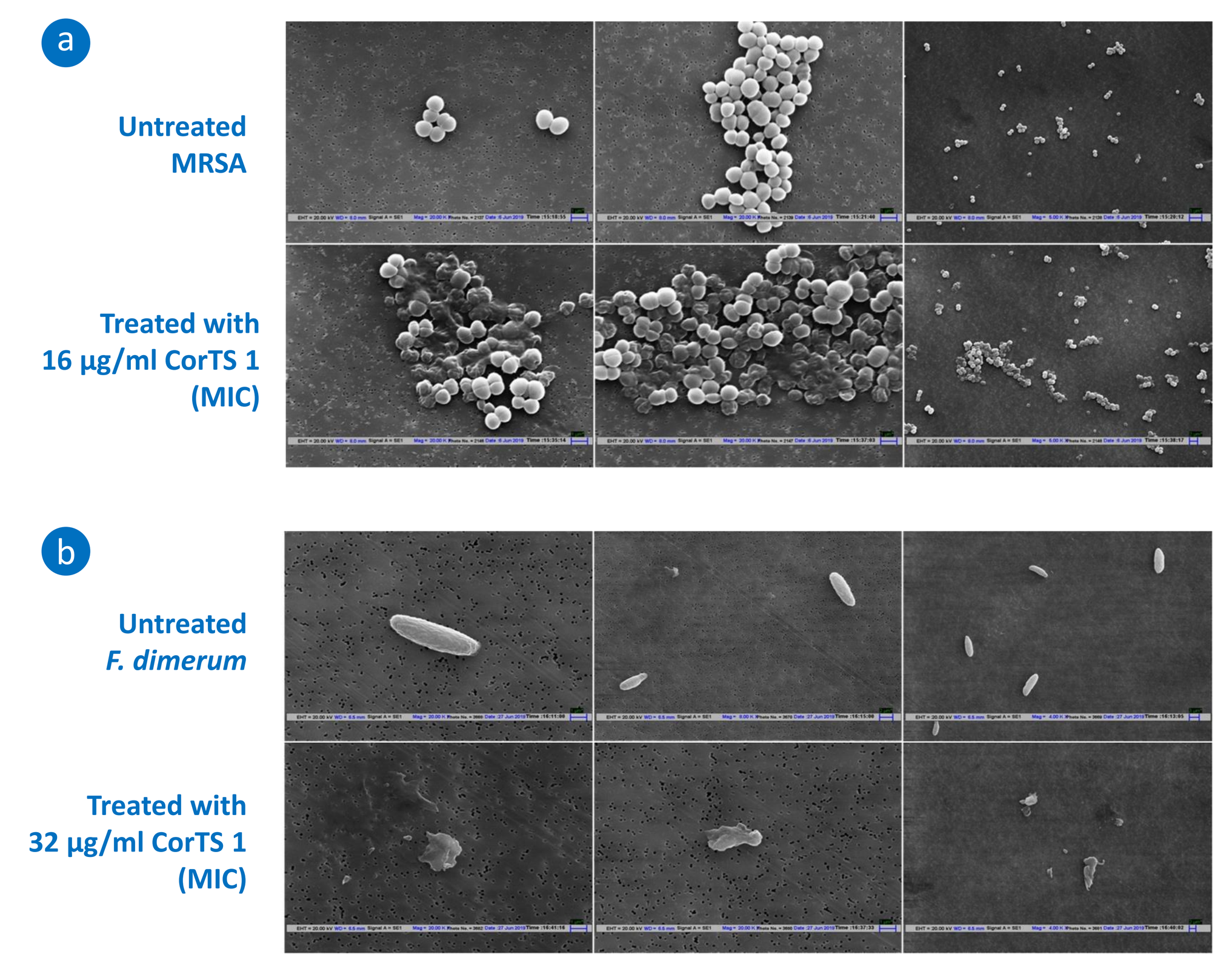

Fig. 5. Scanning electron microscopic analysis of (a) Methicillin-Resistant *Staphylococcus aureus* (MRSA) (b) *Fusarium dimerum* after CorTS 1 treatment.

4. Peptide Localization in Cornea

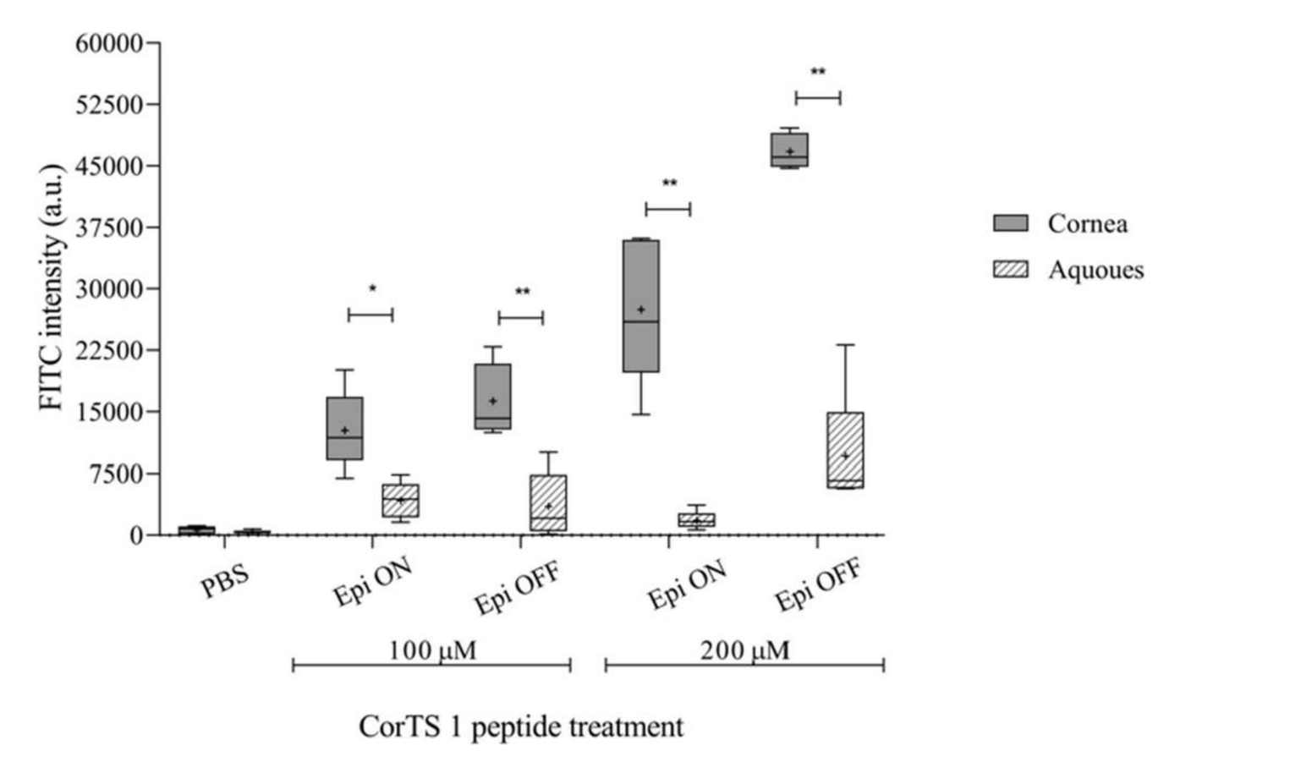

Fig. 6. Fluorometric results of tissue penetration of CorTS 1 after 30 min of topical application in goat eyes with intact epithelium (ON) and debrided epithelium (OFF).

5. Collagen Protective Property Investigation

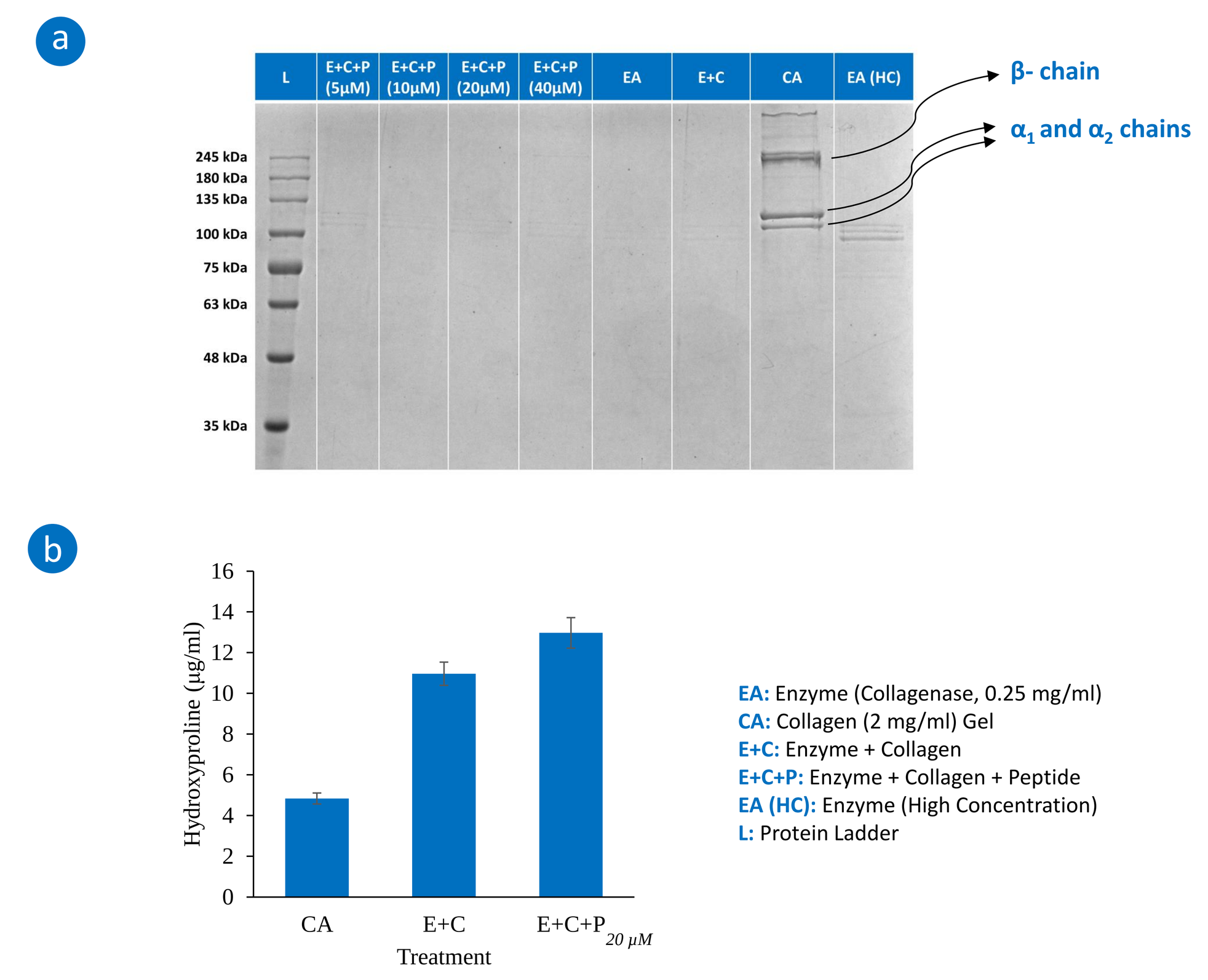

Fig. 7. Analysis of collagen gel digestion by collagenase in presence and absence of peptide by (a) SDS-PAGE profile and (b) Hydroxyproline assay ***(Unpublished Results)***

6. Toxicity Evaluation

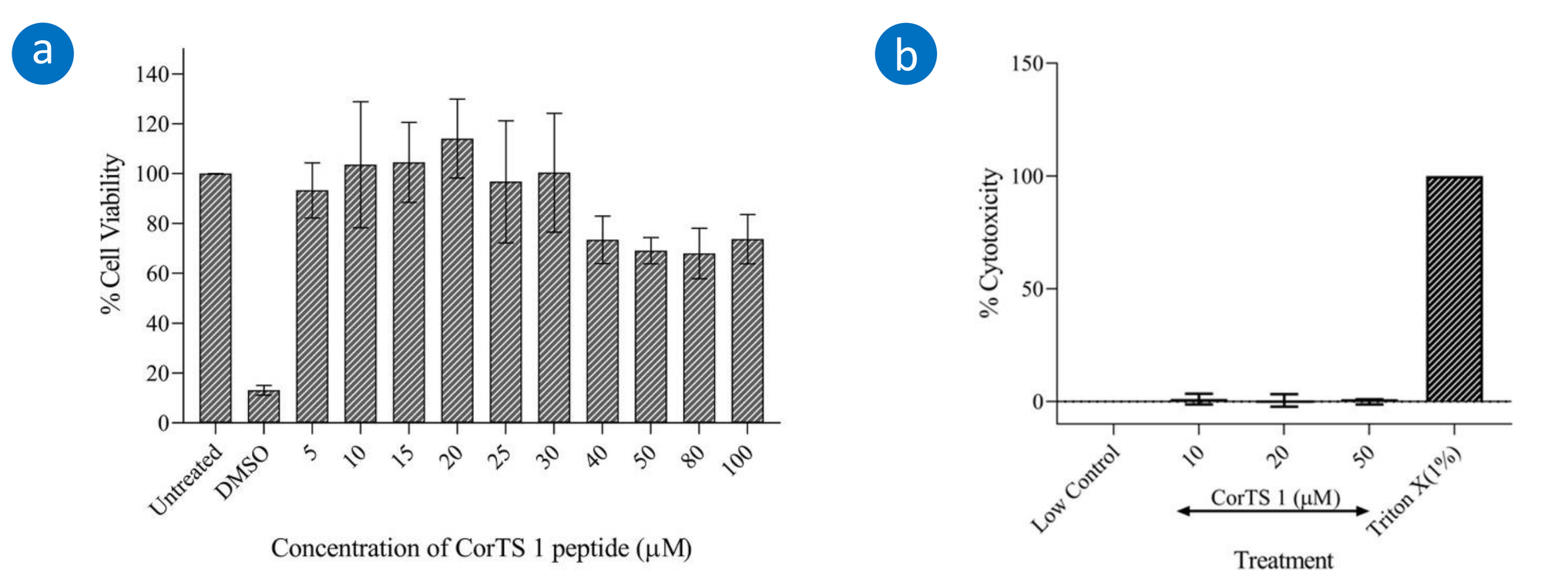

Fig. 8. (a) Percentage viability of HCE cells treated with CorTS 1 for 24 hr evaluated by MTT assay. (b) Percentage cytotoxicity in HCE cells treated with CorTS 1 evaluated by LDH assay.

DISCUSSION AND FUTURE

CorTS-1 is a **cornea targeting cell penetrating peptide** with its localization in cornea.

It has **antimicrobial** effect as well as **collagen interaction** properties with no cytotoxicity towards mammalian cell lines.

Although it is **not able to protect the collagen gel** from collagenase digestion ***in vitro***, it is hypothesized to show anti-collagenolytic effect in complex systems.

Other aspects such as its **matrix metalloproteinase inhibitory activity** needs to be checked before investigation in complex systems.

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