INV-102 Attenuates Nitrogen Mustard-Induced Epithelial-Stromal Separation in Rabbit Corneas

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Nitrogen mustard (NM) is an alkylating agent previously used in chemical warfare. Ocular exposure to NM can cause photophobia, corneal ulceration, and corneal opacity. These effects can be mitigated if countermeasures against NM-induced corneal injuries are developed. In NM-induced corneal injuries, anchoring proteins along the epithelial-stromal junction of the cornea are cleaved by enzymes ADAM17 and MMP9, whose induced activation results in corneal separation. This study tested INV-102, a proprietary compound developed by Invirsa®, against NM-induced corneal injuries. This compound had previously been used experimentally to treat ocular viral infections in rabbit eyes and had promoted healing. Organ-cultured rabbit corneas were exposed to 10µL of 10mM NM with or without 35µL of 1% INV-102, applied 2 hr post-NM exposure. Corneas were divided into four groups: unexposed/untreated, INV-102 only, NM-only, and NM+INV-102. Corneas were collected for analysis at 3 timepoints: 1 day, 3 day, and 7 day post-NM exposure, to track the extent of injury. Epithelial-stromal separations were quantified using H&E imaging. Expression levels of ADAM17 and MMP9 were evaluated via immunofluorescence analysis. At 1 day post-NM exposure, ADAM17 and MMP9 expression levels were high in NM-only samples, but were reduced in samples treated with INV-102 after NM exposure. At 3 day, ADAM17 expression remained high for NM-only samples, and were reduced in samples treated with INV-102 after NM exposure. Also, NM+INV-102 samples saw an approximate 30% reduction in epithelial-stromal separation compared to NM-only samples. At 7 day, ADAM17 and MMP9 expression levels were low for both NM-only and NM+INV-102 samples. In general, INV-102 reduced ADAM17 and MMP9 expression as well as the extent of epithelial-stromal separation 3 days post-NM exposure. Future studies with modified formulations of INV-102 will further elucidate the therapeutic potential of this compound.
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