IN VITRO EFFECTS OF TIGILANOL TIGLATE ON KERATINOCYTE WOUND HEALING RESPONSES

OBJECTIVES

Assess and characterise the mechanisms by which tigilanol tiglate (TT) mediate wound re-epithelialisation, closure and restoration of skin barrier function following tumour destruction.

MATERIALS & METHODS

- ***In vitro* tests:**
  - Scratch assays: evaluation of cell proliferation and migration.
  - Gene expression for keratins, matrix metalloproteinases and cytokines/chemokines.
  - Keratinocytes used in the studies are immortalised human skin keratinocytes (HaCaTs) which are a standard, widely-used experiment model.

RESULTS

- **Tigilanol tiglate stimulates both proliferation and migration of keratinocytes in a standard *in vitro* scratch assay model.**
  - Promotes keratinocyte wound healing response.
- **Responses are dose-dependent and there is a strong suggestion that migration and wound repopulation are stimulated independently of the proliferation effects.**
  - Accelerated re-epithelialisation and wound closure.
- **Expression profiling showed that the TT modulated numerous genes associated with wound healing and that these changes were mediated via protein kinase C.**
  - Induce gene expression to facilitate enhanced wound re-epithelialisation.
- **Short bursts of hyper-proliferative activity induced by TT were evident behind the wound edge keratinocytes in the scratch repopulation assays and this is consistent with the characteristic hyper-proliferative bursts that occur behind migrating keratinocytes at the margins of acute wounds that heal normally.**
  - Promotes keratinocyte hyper-proliferation (but for as shorter time than the prolonged hyper-proliferation associated with chronic wound).
- **Accelerated keratinocyte proliferative/migratory responses and rapid re-epithelialisation are hallmarks of highly regenerative tissues.**

CLINICAL INTEREST

Tigilanol tiglate promotes wound re-epithelialisation at sites of tumour destruction.

REFERENCES

Moses, Boyle, Howard-jones, Errington, Johns, Gordon, Reddell, Steadman, Moseley. Novel epoxy-tiglanes stimulate skin keratinocyte wound healing responses and re-epithelialization via protein kinase C activation. Biochemical Phamacology, 178 (2020) 114048. https://doi.org/10.1016/j.bcp.2020.114048.