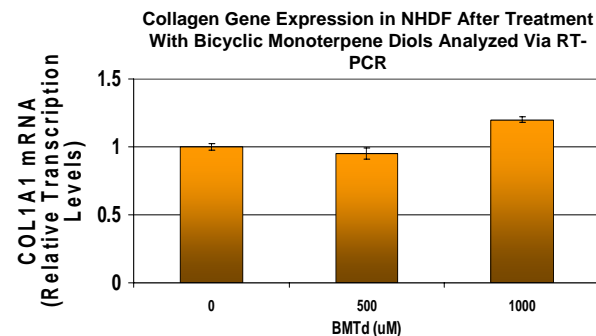
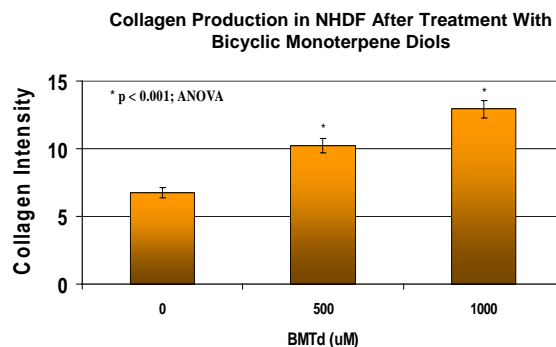


# Bicyclic monoterpene diols increase collagen production and decrease matrix metalloproteinase-1 in fibroblasts

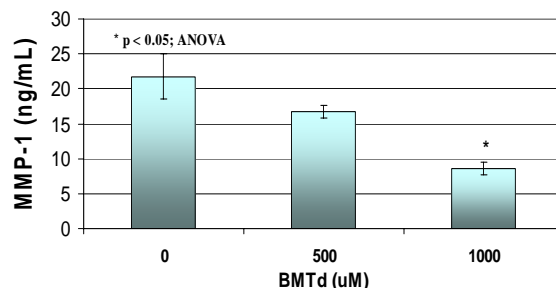
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Bicyclic monoterpene diols (BMTd) increase nitric oxide levels and this pleiotropic mediator was recently reported to increase collagen. This study looked at the direct effects of an equimolar mixture of the BMTd's 2,3-cis/exo-pinenediol and 2,3-cis/exo-camphanediol on both collagen production and expression of a collagenase in normal human dermal fibroblasts (NHDF) treated for 48 hours or 7 days. Collagenases, such as metalloproteinase-1 (MMP-1), degrade collagen and damage the dermal matrix. Treating the NHDF with the BMTd mixture promoted collagen expression and production with increasing doses as measured by RT-PCR, ELISA and immunohistochemistry. There was also a dose-dependent decrease in MMP-1 production as measured by ELISA. To examine metalloproteinase expression controlled indirectly through a paracrine mechanism, conditioned media from normal human epidermal keratinocytes (NHEK) irradiated with UVB and incubated for 24 hrs were transferred to NHDF for 48 hrs. The NHDF were then examined for MMP-1 production. The ELISA results revealed that there was increased MMP-1 production by the NHDF. When conditioned media from NHEK treated with the BMTd mixture for 24 hrs prior to UVB irradiation was transferred to NHDF for 48 hrs, there was a BMTd dose-dependent decrease in MMP-1 production. These results show that the BMTd mixture increases collagen production in fibroblasts and decreases UVB-stimulated MMP-1 in cells both directly and indirectly exposed to the effects of UV irradiation, and suggest that the BMTd mixture may be useful in maintaining high collagen levels within the layers of sun-exposed skin.

Structure of Bicyclic Monoterpene Diols



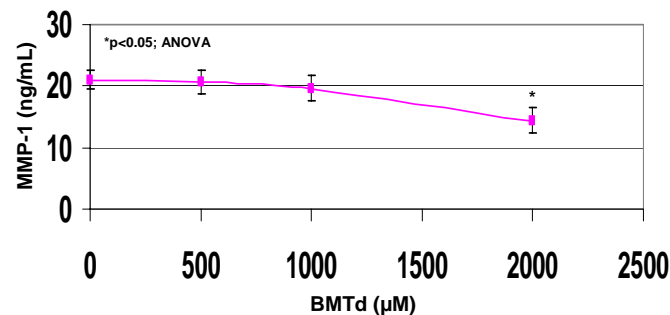
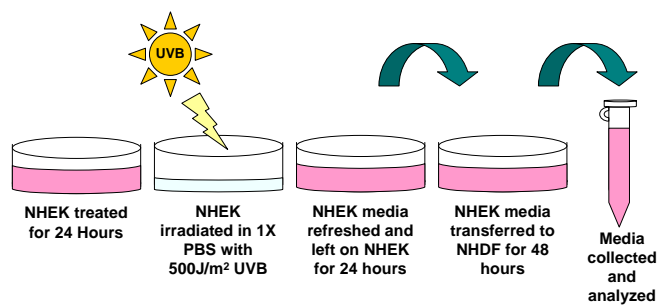
MMP-1 Production in NHDF After Treatment With Bicyclic Monoterpene Diols



## Direct Effects

- NHDF treated with BMTd causes:
  - Collagen to increase
  - MMP-1 to decrease

Metalloproteinase-1 Production in NHDF After Exposure to Media From Keratinocytes Treated With Bicyclic Monoterpene Diols and 500 J/m<sup>2</sup> UVB



## Indirect Effects

- NHDF treated with media from BMTd-treated UVB irradiated NHEK causes:
  - MMP-1 to decrease