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Title: Eugenol enhances proliferation and migration of mouse bone marrow-derived mesenchymal stem cells in vitro

Authors: Sajjad Sisakhtnezhad, Mojdeh Heidari, Ali Bidmeshkipour



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## ACCEPTED MANUSCRIPT

### Eugenol enhances proliferation and migration of mouse bone

#### marrow-derived mesenchymal stem cells in vitro

Sajjad Sisakhtnezhad\*, Mojdeh Heidari, Ali Bidmeshkipour\*

Department of Biology, Faculty of Science, Razi University, Kermanshah, Iran

\* Address for correspondence (Telefax: +98 8334274545; E-mail: s.sisakhtnezhad@razi.ac.ir;

abidmeshki@razi.ac.ir)

Highlights:

- Low concentrations of Eugenol have no toxic effect on BM-MSCs in vitro.
- Eugenol enhances the proliferation and migration of mouse BM-MSCs in vitro.
- Eugenol promotes the migratory potential of MSCs through up-regulation of *c-Met*.
- Eugenol induces MSCs self-renewal through up-regulation of Sox2, Rex1 and Tex10.
- Sox2 may be a hub for the effect of Eugenol on the BM-MSCs.

#### Abstract

Mesenchymal stem cells (MSCs) have received considerable attention in regenerative medicine during the past decade. Eugenol is a natural and versatile vegetable molecule, which has a wide variety of therapeutic effects. Although different biological and pharmaceutical functions of Eugenol are well known, its effect on MSCs has not been studied yet. Therefore, this study was focused on investigating the effect of Eugenol on the proliferation and migration of bone marrow (BM)-derived MSCs in vitro. To do so, BM-MSCs were isolated from 4 to 8 weeks old NMRI mice. Cytotoxicity of Eugenol on MSCs was evaluated by MTT assay at 24, 48 and 72h after treatment. In addition, its effect was assessed on the proliferation and migration of MSCs using wound healing assay in vitro and quantitative gene expression analysis for *Oct4*, *Sox2*, *Cyclin-D1*, *Rex1*, *Tex10*, *Cxcr4*, *Vla4* and *c-Met*. Results showed that Eugenol reduced the number of MSCs in a dose- and time-dependent manner. The median inhibition concentration of Eugenol on MSCs was **400 μg/ml** at 24 and 48h and **200 μg/ml** at 72h after treatment. Moreover, about 90% viability

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