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LETTER

Response to Article "Combined Silver Sulfadiazine Nanosuspension with Thermosensitive Hydrogel: An Effective Antibacterial Treatment for Wound Healing in an Animal Model" [Letter]

Putri Reno Intan [1,*], Ariyani Noviantari [1,*], Sukmayati Alegantina [2,*]

[1]Center for Biomedical Research, Research Organization for Health, National Research and Innovation Agency (BRIN), Cibinong Science Center, Cibinong - Bogor, West Java, Indonesia; [2]Research Center for Pharmaceutical Ingredients and Traditional Medicine, Research Organization for Health, National Research and Innovation Agency (BRIN), Cibinong Science Center, Cibinong - Bogor, West Java, Indonesia

*These authors contributed equally to this work

Correspondence: Putri Reno Intan, Center for Biomedical Research, Research Organization for Health, National Research and Innovation Agency (BRIN), Genomic Building, Cibinong Science Center, Jalan Raya Bogor Km. 46, Cibinong – Bogor, West Java, 16911, Indonesia, Email putri.reno.intan@brin.go.id

Dear editor

We appreciate the authors publishing their research "Combined Silver Sulfadiazine Nanosuspension with Thermosensitive Hydrogel: An Effective Antibacterial Treatment for Wound Healing in an Animal Model" in International Journal of Nanomedicine:18, 679–691.[1] This information is crucial to understand the effectiveness of nanosized silver sulfadiazine loaded in poloxamer thermosensitive hydrogel (NS/Gel) and its safety in vivo.

Pseudomonas aeruginosa, Staphylococcus aureus, and *methicillin-resistant S. aureus* (MRSA) are the most common microbial strains found in patients with infected wounds. Metal nanoparticles (NPs) like zinc (Zn), silver (Ag), and gold (Au) have bacteriostatic/bactericidal activity including low in vivo toxicity and they are suggested wound dressings.[2] Previous study reported that the combination of silver sulfadiazine (AgSD) nanosuspensions and thermoresponsive hydrogel decreased cytotoxicity using the methyl thiazolyltetrazolium (MTT) assay in the L929 mouse fibroblast cell lines and improved AgSD antibacterial activity in vitro.[3] In this letter, we would to communicate our thoughts on the staining method used to examine the inflammation response in this study.

In this paper, the author mentioned that transforming growth factor β (TGF-β), vascular endothelial growth factor A (VEGF-A), and interleukin 6 (IL-6) are mainly evolved during three phases of wound healing, which include the inflammatory stage, granulation tissue formation, and collagen fiber production. TGF-β can regulate wound healing and fibrosis by increasing the expression of collagen type I. VEGF-A plays a role in vasculogenesis by promoting metabolic activity for cell proliferation and collagen synthesis. Furthermore, IL-6 indicated an inflammatory response following wound induction. Lei et al reported that growth factors are secreted into injured areas to regulate cellular responses during the healing process of wounds. These responses include promoting angiogenesis, re-epithelialization, and reducing the inflammatory response. Concerning IL-6, tumor necrosis factor α (TNF-α) is another marker of inflammation.[4]

Treatment for skin wounds aims to minimize the formation of scar tissue, promote quick wound healing, and restore the natural tissue structure and functioning of damaged skin. As a result, more specifics of wound repair under various circumstances were assessed in rat model studies. Skin wounds are frequently vulnerable to microbes that could cause inflammation and so inhibit the healing process. In this paper, the author reported that to measure the cytokines, they used Enzyme-Linked Immunosorbent Assay (ELISA). IL-6 expression increased on the first day, then decreased over the next few days. The increase in IL-6 expression indicated an inflammatory response following wound induction.

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Preferably, immunohistochemistry (IHC) or immunofluorescence (IF) are provided for the cytokine analysis method used in wound healing with ELISA to detect the presence and location of a specific protein in the cells or the tissue. The limitations of ELISA involve unskilled labour and expensive antibody preparation, advanced techniques, a high possibility of false positives and negatives, inadequate blocking of immobilized antigen yields false results, antibody instability, and the necessity of refrigerated transport and storage because antibodies are proteins.[5]

Lei et al evaluated wound healing using IHC staining of inflammatory factors like TNF-α and IL-6. The expression of this marker was greatly reduced on day 9. Silver, ZnO, copper, gold, other metals, and metal oxide nanoparticles can be added to chitosan hydrogels to improve their antibacterial properties.[4] Domizio et al reported that skin injury causes dermal cells to produce growth factors. Immunofluorescence analysis using confocal microscopy confirmed this finding by showing colocalization of CXCL-10 with neutrophils infiltrating the skin at early time points post-injury, also the expression of TGF-β in macrophages, and fibroblast growth factor 2 (FGF-2) in fibroblasts.[6]

Analysis of IHC was utilized to measure the amounts of TNF-α and IL-6, two markers of inflammation, in the wound tissues to assess the degree of inflammation variation in wounds.[7] Besides that, another IHC staining used to determine the presence of neutrophils is anti-neutrophil elastase (NE) from skin samples of burn wounds.[8,9]

As a result, the TNF-α and IL-6 staining to investigate the inflammatory response may be taken into consideration for use soon to continue this investigation. Generally, this study still represents the original idea of investigating an antibacterial treatment for wound healing using a thermosensitive gel in combination with silver sulfadiazine nanosuspension, which may be further investigated and analyzed to solve the suggestions made above.

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Disclosure

There are no conflicts of interest with the communication, based on all authors.

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