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PROCEEDINGS ABSTRACT

Pharmacological approach to tooth regeneration *via* uterine sensitization-associated gene-1 inhibition

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Oral diseases remain a major global public health burden. Although oral healthcare has improved in many regions, common conditions such as dental caries and periodontal disease continue to be highly prevalent. These disorders frequently result in tooth loss and negatively impact overall health, quality of life, and well-being. Current treatments such as dental implants are widely considered as standard treatment for the replacement of missing teeth. However, they do not actually restore a real biological tooth and they are associated with several complications; amongst these, peri-implantitis is the most significant and is characterized by an inflammatory destruction of peri-implant tissues and progressive bone loss, ultimately leading to implant failure. These limitations highlight the need for effective pharmacological strategies that promote true biological tooth regeneration [1]. Recent studies have focused on a protein called "uterine sensitization–associated gene-1" (USAG-1), which is known to suppress tooth development by blocking signalling pathways such as those of the bone morphogenetic protein (BMP) and Wnt [2]. When USAG-1 was inhibited in animal studies, *de novo* tooth formation was observed. From a pharmacological perspective, USAG-1 represents a potential therapeutic target for the induction of tooth regeneration. Experimental approaches such as monoclonal antibody therapy (widely used in cancer therapy to target specific proteins involved in disease progression) and RNA-based gene silencing have been shown to decrease USAG-1 activity, thereby restoring Wnt and BMP signalling and reactivating the dormant odontogenic potential [3]. Similarly to other vertebrate organs, tooth development (odontogenesis) is known to be regulated by reciprocal interactions between epithelial and underlying mesenchymal tissues through multiple signalling pathways, including the Wnt and BMP ones. More specifically, the Wnt signalling is activated at the earliest stage of odontogenesis and is responsible for initiating tooth formation by activating odontogenic stem cells and promoting the formation of the tooth bud through increased cellular proliferation. In contrast, the BMP signalling becomes more prominent during later stages, where it regulates cellular differentiation and guides the formation of specialized dental cells (such as ameloblasts and odontoblasts) responsible for enamel and dentin formation. Although USAG-1-targeting therapies are not yet clinically available, they represent a promising area of pharmaceutical research, in which pharmacists play a key role in drug development, safety evaluation, and future clinical application(s). However, several limitations must be considered. Most current evidence is based only on animal models; therefore, the inhibition of USAG-1 in humans remains uncertain. In addition, the long-term safety of monoclonal antibody or RNA-based therapies also requires further investigation, particularly in light of the known adverse effects associated with biologic therapies. Moreover, RNA-based approaches face important

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challenges related to effective drug delivery and optimal dosing strategies. Therefore, additional preclinical and clinical investigations are required in order to assess the safety, efficacy, and feasibility of USAG-1 inhibition before any relevant therapeutic strategies can be successfully introduced into clinical practice.

Keywords

BMP; drug development; oral diseases; tooth regeneration; USAG-1

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Conflicts of interest statement

None to declare.

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