NEW MOLECULES FOR BONE TISSUE REGENERATION

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Invention

The present invention concerns the development of new pharmacologically active compounds for the **treatment of osteoporosis and in general bone diseases** characterized by progressive loss of bone mass, such as rheumatoid arthritis, hyperparathyroidism, and bone cancer metastases.

The invention consists of a **new class of original molecules**, structurally related to the class of bisphosphonates, currently used in the treatment of osteoporosis, but possessing multiple mechanisms of action. They have, in fact, been shown to be able to:

1) inhibit osteoclastic function (bone catabolism);

2) stimulate osteoblastic function (bone anabolism);

3) exert anti-inflammatory action;

4) exert pain-relieving action;

5) exhibit significantly reduced cytotoxicity compared with related reference drugs.

Drawings
& pictures

Health Bone

Bone with osteoporosis

Industrial applications

The pharmacological class covered by the invention represents an innovative and wholly original pharmacotherapeutic approach for the treatment of important and widespread diseases of the **osteoarticular system**, such as **osteoporosis and osteoarthritis**.

To date, the therapeutic approach for the prevention and treatment of osteoporosis-induced bone fragility is the use of drugs that **inhibit bone resorption**, that is bone breakdown caused by osteoclastic activity. The reference class of drugs in this category is bisphosphonates; their mechanism of action, however, does not induce the reconstitution of already lost bone mass. In addition, the inhibition of osteoclast results in prolonged suppression of the physiological mechanisms that control bone turnover, possibly leading to increased bone fragility due to simultaneous suppression of bone neoformation due to the "coupling" effect.

Thus, the patented molecules aim to address the **clinical need to develop new drugs that can stimulate the physiological mechanisms of turnover rather than inhibit them**.

Possible developments

The inventors, who are experts in pharmaceutical chemistry and pharmacology, turned their attention toward the biological role of Hydrogen Sulfide (H_2S), that, acting as a gas-transmitter, exerts various effects on cells and tissues including cytoprotective, antioxidant, anti-inflammatory and vasodilation inducing effects. In preliminary studies, the inventors noted the relevant ability of H_2S to modulate the function and phenotypic differentiation of human bone cells, useful in the process of bone remodeling. Based on these studies, they designed and developed a novel class of compounds that exhibits a multiple mechanism of action, not exhibited by other drugs currently available in the clinical practice, and in particular by the drug selected as a reference, Alendronate.

In vitro tests were performed on primary cell cultures of the osteoarticular system (osteoblasts and osteoclasts), obtained from explants, demonstrating lower cytotoxicity and additional pharmacological properties compared to the reference drug. These were carried out at the Istituto Ortopedico Rizzoli, a co-owner of the patent.

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