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(54) Title: N-HYDROXY-2-(ALKYL, ARYL, OR HETEROARYL SULFANYL, SULFINYL OR SULFONYL)-3-SUBSTITUTED ALKYL, ARYL OR HETEROARYLAMIDES AS MATRIX METALLOPROTEINASE INHIBITORS

(57) Abstract

Matrix metalloproteinases (MMPs) are a group of enzymes that have been implicated in the pathological destruction of connective tissue and basement membranes. These zinc containing endopeptidases consist of several subsets of enzymes including collagenases, stromelysins and gelatinases. TNF- α converting enzymes (TACE), a pro-inflammatory cytokine, catalyze the formation of TNF- α from membrane-bound TNF- α precursor protein. It is expected that small molecule inhibitors of MMPs and TACE therefore have the potential for treating a variety of disease states. The present invention provides low molecular weight, non-peptide inhibitors of matrix metalloproteinases (MMPs) and TNF- α converting enzyme (TACE) for the treatment of arthritis, tumor metastasis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, diabetes (insulin resistance) and HIV infection. The compounds of this invention are represented by formula (I), where R¹, R², R³ and R⁴ are described herein.

