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Natural Products as Inhibitors of Matrix Metalloproteinases

Pankaj Gupta*

School of Medical and Allied Sciences, KR Mangalam University, Sohna Road, Gurgaon, Haryana, India

Matrix metalloproteinases (MMPs) also known as matrixins are a family of zinc metallo-endopeptidases secreted by cells and are responsible for much of the turnover of the matrix components. It is included in the "MB clan" of metallopeptidases containing the motif *HEXXHXXGXXH* as the zinc binding active site. They were first described in vertebrates in 1962 including Homo sapiens and later in non-vertebrate members such as sea urchins, soybeans, *Caenorrhabdita elegans* and *Arabidopsis thaliana* [1]. Matrixins consists of 26 members ranging from MMP-1 to MMP-28 including the membrane type matrix metalloproteinases and belong to the metzincin superfamily.

They are involved in various biological processes such as wound healing, angiogenesis, apoptosis, embryonic development, organ morphogenesis etc. and several matrix metalloproteinases have also found expression in various pathological conditions such as cancer, corneal ulceration, skin ulceration, neurological disease, arthritis, fibrotic lung diseases etc. Matrix metalloproteinases are inhibited by several endogenous tissue inhibitors of metalloproteinases (TIMPs) such as TIMPs (1-4). Pathological conditions require exogenous MMP inhibitors that may be of natural or synthetic origin. Synthetic inhibitors of MMPs include doxycycline, marimastat, trocade, etc.

Several compounds from natural sources have shown promising inhibition of matrix metalloproteinases particularly some flavonoids, alkaloids and phenolic compounds from plant sources e.g., phenolic compounds from *Emblica officinalis* exhibited inhibition of MMP-1, curcumin from *Curcuma longa* showed inhibition of MMP-2 and MMP-14, flavonoids from *Passiflora foetida* profoundly inhibited MMP-1, polyphenols from *Camellia sinensis* exhibited inhibition of MMP-1, MMP-2, MMP-3, MMP-7 and MMP-9 thereby exhibiting their potential for the prevention of photoaging [2]. A number of compounds from marine sources have also shown profound inhibition of MMPs such as Ageladine A from the marine sponge *Agelas nakamurai* exhibited inhibition of MMP-1, MMP-2, MMP-8, MMP-9, MMP-12, and MMP-13. Fucoidan extracts from seaweeds *Claisiphon novae-caledoniae* and methanolic extracts from marine red algae *Cavalina pilulifera* showed inhibitiion of MMP-2 and MMP-9 implicating its anti-photoaging potential [3]. However, the need for more potent and highly selective inhibitors of matrix metalloproteinases remains a mainstay requiring the exploration of more natural products for the cure of pathological conditions expressing MMPs.

References

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***Corresponding author:** Pankaj Gupta, Assistant Professor, School of Medical and Allied Sciences, K.R. Mangalam University, Sohna Road, Gurgaon-122 103, Haryana, India, Tel: +91119818256122; E-mail: gupta.aiims@gmail.com

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