SymMatrix - a New Skin-firming Active from Blackberry

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Through aging, the balance of synthesis and degradation of cutaneous extracellular matrix (ECM) proteins necessary for skin integrity and tissue regeneration becomes impaired (1). At the histological level, the dermis shows a general loss of ECM reflected by a decreased number of fibroblasts, reduced levels of collagen and elastin as well as impaired organisation of collagen fibrils and elastic fibers resulting in wrinkle formation and loss of elasticity and firmness. Matrix metalloproteinases (MMPs), a group of structurally related enzymes that degrade ECM proteins, play a major role in this process (2).

In the skin, MMPs are produced by various cell types like keratinocytes, fibroblasts, macrophages, endothelial cells, mast cells, eosinophils, and neutrophils. They are mostly secreted as the inactive form (pro-MMP) which needs activation to gain its proteolytic functionality. MMPs have a broad and often overlapping substrate specificity (table 1) and together they are capable of degrading all components of the ECM. The regulation of MMP activity occurs at various levels: gene transcription, activation of the pro-enzyme by a cascade of enyzmes comprising serine proteases like human leukocyte elastase (HLE) and other MMPs and finally inactivation by inhibitors (3).

With aging, MMP levels increase in the skin as was shown by comparison of old and young skin resulting in excess proteolytic activity (2). Various factors like UV and infrared radiation, tobacco smoke, and environmental toxins like ozone induce MMPs in human skin leading to premature skin aging (4-7). In addition to the age-related enhancement of MMP levels, the production of tissue inhibitors of metalloproteinases (TIMPs), their specific inhibitors, was found to be decreased (8).

MMP inhibitors thus provide an efficient tool to prevent this excess destruction of matrix proteins and thereby help the depleted skin's regulation systems. They not only inhibit the active MMP but may also interfere with the activation of the latent pro-MMP. As described above, activation of the pro-enzyme is achieved by a cascade of enzymes including not only other MMPs but also such serine proteases as HLE. Thus, further benefit will be obtained by the usage of a multifunctional inhibitor.

Here, we report about such a multifunctional inhibitor: SymMatrix, a new skin-firming active derived from blackberry leaves.

Phytochemical characterization of blackberry leaf extract

Blackberry (Rubus fruticosus) is a member of the rose family (Rosaceae). Native to Europe and North America, blackberry now grows in many temperate regions. It is a weedy, fast growing shrub with thorny leaves and twigs (figure 1). Blackberries are also cultivated and meanwhile several thornless varieties are available. They are mainly grown for their aromatic black or dark purple fruits which are edible raw or cooked. Blackberry leaves are used in traditional medicine. Both, the tea and the decoction

Protease	Synonyms	Known substrates
MMP-1	Interstitial Collagenase, Collagenase-1, Fibroblast Collagenase	Collagen type I, II, III, VII, VIII and X, gelatin, aggrecan, versican, pro-TNF, pro-MMP-2, pro-MMP-9
MMP-2	Gelatinase A, 72-kDa Gelatinase, Type IV Collagenase	Collagen type I, IV, V, VII, X, XI and XIV, gelatin, elastin, fibronectin, aggrecan, versican, pro-TNF, pro-MMP-9, pro-MMP-13
MMP-3	Stromelysin-1	Collagen type III, IV, IX and X, gelatin, aggrecan, versican, fibronectin, laminin, elastin, fibrinogen, pro-TNF, pro-MMP-1, pro-MMP-7, pro-MMP-8, pro-MMP-9, pro-MMP-13
MMP-9	Gelatinase B, 92-kDa Gelatinase, Type IV Collagenase	Collagen type IV, V, VII, X and XIV, gelatin, elastin, aggrecan, versican, fibronectin, pro-TNF

Table 1: Selected matrix metalloproteinases (MMPs) secreted from skin fibroblasts and/or keratinocytes and their substrate specifity